Short Communication

Experience of GLP-1 agonist Exenatide in the management of type 2 diabetic obese Pakistani patients

Osama Ishtiaq, Rida Kamal, Tahir Iqbal, Batool Zahra

Department of Medicine, Shifa International Hospital and Shifa College of Medicine, Islamabad and Lahore Medical and Dental College, Lahore, Pakistan

Objective: We evaluated the use of Exenatide in terms of weight reduction and improvement of glycemic control, in patients with type 2 diabetes and obesity from Pakistan. **Methodology:** The study was done in Shifa International Hospital, Islamabad from year 2013 to 2014. Exenatide was prescribed to 45 patients, in which 19 patients had completed follow-ups. HbA1c, BMI and weight were recorded before and after the treatment. Side effects and reason for early discontinuation were also noted. **Results**: The concurrent use of Exenatide along with other anti-diabetic medications, enabled patients to reduce an average weight of 6.6kg (average decrease in BMI was 1.82kg/m2) and HbA1c levels of 0.6% over a period of 5 months, making it a promising therapeutic agent in obese and diabetic patients. The most common side effect noted was nausea. **Conclusion:** Exenatide has a potential to achieve reasonable weight loss and mild improvements in glycemic control in Pakistani obese and diabetic patients. (Rawal Med J 201;41:519-521)

Keywords: Exenatide, diabetes mellitus, obesity, GLP-1 agonist.

The global epidemic of obesity is responsible for greater number of deaths than under nutrition. Except bariatric surgery, no medical therapy provides an intensive treatment for obesity. However, this treatment is not suitable for all patients.[1] Thus, optimal pharmacological strategies are being explored which can have modest efficacy. Exenatide is a glucagon like peptide 1 agonist belonging to the group of incretin mimetics. It is a subcutaneous injection, usually used with other anti diabetic medication for better control of glucose levels in diabetic patients.[2] Beside, improvement in the glycemic control, it also helps in weight reduction as well and is an important indication to use it in obese diabetic patients.

To our knowledge, Exenatide has not been studied in the Pakistani patients previously. We retrospectively reevaluated obese and diabetic patients who were prescribed Exenatide for their diabetes control with added weight loss. The study was done in Shifa International Hospital, Islamabad from year 2013 to 2014. Exenatide was prescribed to 45 patients, in which 19 completed follow-ups. It was given in a limited number of patients due to its high cost and the subsequent affordability restrictions. The study was approved by Institutional Ethical Review Board.

All patients were obese and had type 2 diabetes mellitus. Exenatide was primarily given to reduce weight and improvement in the diabetes control. However, in 26% of patients who had good glycemic control (HbA1c below 7%), it was given with an aim to reduce weight.

Patients were evaluated for BMI and HbA1c levels before and after Exenatide over an average duration of nine months. All patients were simultaneously doing regular physical exercise and following dietary restrictions and were on oral medications, while 37% (n=7) were using insulin in-addition, for their diabetes control.

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The average duration of use of Exenatide by patients was 5 months with an average dose of 15mg per day. During the course of study, 74% of the patients lost weight. The average weight loss recorded was 6.6kg. The greatest achievement of the study was observed with maximum weight reduction of 21kgs was achieved over a period of 11 months with Exenatide 10mg daily used with three other oral hypoglycemic (Table 1). Twenty five percent

patients had no change in their weight and 1% gained 2kgs. With reduction in weight, average decrease in BMI was 1.82 kg/m2. HbA1c levels had an average decrease of 0.6% in 55% of the patients. Maximum reduction was 1.2% over a period of 4.5 months with Exenatide 10mg per day along with insulin and 2 other oral hypoglycemics. The levels remained same in 28% of patients. Seventeen percent of the patients obtained greater reading with an average increase of 1.13%. None of the patients had any reduction in their other medications during and after the use of Exenatide.

Table 1. Characteristics of patients treated with Exenatide.

Age / Gender	52 years: 12.8 SD	
Gender	Males: 10 (52.6%) Females: 9	
Reason to Start	Diabetes Control Diabetes and Obesity	74% 100%
Pre-start Medications	Oral Medications One OAD / Two OAD / Three OAD / Insulin	18 (95%) 10 (53%) / 6 (31%) / 3 (16%) 7 (37%)
Duration of treatment	4.7 months : 4.8 SD	
Dose of Byetta	15mg	
Reason for Stopping the medication *	No Benefit No Follow up Side Effects	42% 26% 26%
Side Effects	Nausea and lethargy Renal Failure	99% 5.3%

OAD = Oral anti-diabetic drugs, SD = Standard Deviation
* Others patients continued using Exenatide even after the completion of study

Table 2. Benefits of Exenatide before and after the study.

	Before the treatment		After the treatment		P *
Weight (Kg)	111.50	18.45 SD	106.74	18.51 SD	0.225
BMI (kg/m2)	40.53	6.83 SD	38.71	6.5 SD	0.001
HbA1c	8.11%	2.1 SD	7.97%	2.25 SD	0.001

SD = Standard Deviation, BMI = Body Mass Index
* P value was calucated using Paired T-test.

Fourty two percent (42%) of the patients found no benefit with the usage whereas only five percent (5%) of the patients successfully achieved the desired weight (Table 2). The rest did not follow up or discontinued due to side effects. Of the 26% users who discontinued, Exenatide due to side effects, the most common reported was severe nausea and lethargy. Moreover, one patient developed acute renal failure with creatinine rising to 2.8mg/dl from 1mg/dl over a period of 1 month, which led to the discontinuation of drug. Patient's renal functions recovered within a month when the drug was withdrawn.

There is abundant evidence that administration of GLP-1 agonist improves metabolic conditions of the body, as supported by our study. A review of 51 randomized controlled trials concluded that GLP-1 agonists are a favorable drug for weight control in patients with type 2 diabetes[3] when compared with traditional oral hypoglycemic as seen in this study. Another review stated its advantages in decreasing HbA1c levels, fasting plasma glucose levels and body weight.[4] Producing similar results, a study proved Exenatide as an effective therapy for improving glycemic control, HbA1c, lipid profile, BMI and blood pressure.[5] Comparing to DPP4 inhibitors, Russell S reviewed 18 clinical trials and concluded that GLP-1 agonists help in achieving greater reductions in HbA1c with better patient satisfaction and lower incidence of hypoglycemia.[6] A randomized controlled trial compared glimepiride with Exenatide in patients with inadequately controlled glucose levels who were previously using metformin only. The results showed significant decrease in HbA1c levels and body weight in the group of patients using Exenatide,[7] which correspond to the findings of this study.

Our results are similar to prior studies and favors Exenatide as a potential drug to reach desired metabolic goals in Pakistani obese and diabetic patients. The limitations encountered by our study were limited sample size and duration of treatment.

Author Contributions:
Conception and design: Osama Ishtiaq
Collection and assembly of data: Osama Ishtiaq, Rida Kamal, Batool Zahra
Analysis and interpretation of the data: Osama Ishtiaq, Rida Kamal
Drafting of the article: Rida Kamal, Osama Ishtiaq
Critical revision of the article for important intellectual content: Osama Ishtiaq
Statistical expertise: Osama Ishtiaq
Final approval and guarantor of the article: Tahir Iqbal
Corresponding author email: Dr. Osama Ishtiaq: docosama@gmail.com
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