

# Successful Management of Extremely Insulin-Resistant Obese Diabetic Patient with Insulin Glargine, U-500 Regular Insulin and Pramlintide

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## Abstract

Treating diabetes in obese patients is extremely challenging. Recently, physician's use of U-500 regular insulin has increased to treat diabetes in this population. Here we report the use of the combination – insulin glargine, U-500 regular insulin and pramlintide to successfully manage type 2 diabetes in an extremely obese patient with a BMI of 54, A1C of 10.6 and a C-peptide level of 3.5 that indicated insulin resistance. With use of this combination of three drugs we were able to reduce the total number of drugs needed to manage patient's diabetes from five to three, thereby also improving the likelihood of compliance.

**Keywords:** Diabetes; Insulin glargine; Obese; U-500 insulin; Pramlintide

## Introduction

Type 2 diabetes is characterized by insulin resistance and progressive beta cell dysfunction, resulting in deficiencies of both insulin and amylin, as the disease progresses. Increased obesity in the population has led to increased number of diabetic patients whose diabetes cannot be adequately controlled by conventional methods. Managing type II diabetes of extremely obese patient is challenging [1] and several different approaches have been used recently to address this problem.

Riddle et al. [2] have reported that when pramlintide, an amylin analogue, was used in combination with insulin glargine, a basal insulin preparation, to manage patient's diabetes, improved glycemic control was also accompanied by weight loss.

Davidson et al. [3] substituted U-500 regular insulin for U-100 NPH insulin and found marked improvement in diabetes control in obese, severely insulin resistant type 2 diabetic patients. Lane et al [4] have used a combination of U-500 with liraglutide, glucagon-like peptide agonist, for better diabetic management outcome.

In our literature search, we searched Pub Med for articles containing the terms, U-500 insulin and insulin glargine (retrieved -7 citations) or pramlintide and insulin glargine (retrieved -11 citations). Pub Med search indicating all three agents together yielded zero citations. In this communication, we report a case of successful management of highly obese, insulin resistant, type 2 diabetic patient's diabetes by using these three agents- U-500 insulin, pramlintide and insulin glargine.

## Case Report

### Patient information

DS is a 29-year-old female, who had uncontrolled type 2 diabetes for last five years. She is 5' 10" tall, weighs 335 pounds and has a BMI of 54. Her primary care physician diagnosed DS as type 2 diabetic, after completing both a 2-hr OGTT as well as A1C. Further confirmation of her insulin-resistant status was established, when a c-peptide value of 3.5 ng/ml was obtained six weeks later. DS's comprehensive lab summary for past eighteen months is shown in (Table 2). When the patient was first seen at this clinic in November of 2009, patient's weight was 307 pound and A1c 10.6%. Her diabetes was managed with bedtime insulin glargine and insulin lispro sliding scale.

## Investigation

In January 2010, insulin glargine bed time dose was changed to 44 units BID, and sitagliptin 100 mg added to her therapeutic regimen. By February 2010, A1c value dropped by 2 units to 8.6% accompanied by a 2.4 pound decrease in weight. During the next six months, insulin glargine was titrated upwards to 75 units BID, while patient continued on insulin lispro sliding scale and sitagliptin. On August 9, 2010, her A1c was 9% and weight 305 pounds. During this visit pramlintide 120 mcg injection three times daily was added to patient's regimen. By December of 2010, patient's insulin glargine requirement was 85 units BID, weight 341 pounds, an increase of 34 pounds within a year, and A1C was still well above normal at 8.6%.

It was at this point, exenatide 10 mg BID was added to patient's profile. During 6 weeks in this regimen of insulin glargine, insulin lispro (s/s), sitagliptin, pramlintide and exenatide, patient's weight dropped by 26 pounds and A1c to 7.5%. But at this point, doses of insulin glargine became so high that patient herself could observe insulin stacking. Abrupt release of this insulin had caused an incident of hypoglycemia.

At this point insulin lispro sliding was replaced by U500 regular insulin, 60 units before meals, and exenatide discontinued from her regimen, as its use with insulin is contraindicated. During the course of next three months, patient's A1c dropped to 7.1%, but patient has gained eight pounds to weigh 322 pounds.

As this patient is young and has been struggling to manage her diabetes for past several years, we are pleased that with this combination of three drugs-pramlintide, U500-insulin and insulin glargine, her diabetes is under control and patient is feeling better. We will continue

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Date	Insulin glargine dose	Weight [pounds]	A1C	Drug(s) added (+) or discontinued (-) at this visit
Jan 2010	44 U BID	306.4		+ Sitagliptin 100 mg
Feb 2010		304	8.6	
Aug 2010	75 U BID	305	9	+ Pramlintide 120 mcg inj. TID
Dec 2010	85 U BID	341	8.6	+ Exenatide 10 mg BID
Feb 2011		314	7.5	+ U-500 insulin 60 U AC - Exenatide - Sitagliptin
May 2011		322	7.1	

**Table 1:** Patient's therapeutic management.

Date	05/16/11	02/16/11	11/10/10	08/06/10	02/23/10
Parameter					
HbA1c [%]	7.1 (H)	7.5 (H)	8.6 (H)	9 (H)	8.6 (H)
Chol (mg/dL)	112	107	109	175	127
HDL [mg/dL]	34 (L)	31 (L)	29 (L)	30 (L)	29 (L)
LDL [mg/dL]	56	63	58	116 (H)	81
Trig [mg/dL]	111	66	112	146	127
K [mmol/L]	4.7	4.2	4.6	4.1	-
ALT [units/L]	34	32	43 (H)	49 (H)	-
AST [units/L]	21	28	39 (H)	36 (H)	
Creat [mg/dL]	0.58	0.6	0.64	0.59	0.7
eGFR [ml/min]	109	60	-	60	-

**Table 2:** Patient DS's laboratory data summary.

to follow this patient on how this regimen is able to control her diabetes over the long run.

## Conclusions

Management of diabetes in extremely obese patient is challenging. While other investigators have reported decrease in patient weight with U-500 regular insulin [4], increased weight observed in this patient was related to occurrence of edema as result of herpes infection, which was controlled by furosemide. By judicious use of these three drugs-insulin glargine, U-500 insulin and pramlinitide, total number of drugs patient needed to control her diabetes has been reduced from 5 to 3 and the A1C is reduced from 10.6% to 7.1%. Patient original medications were- exenatide, simvastatin, insulin lispro, sitagliptin, insulin glargine and the current three medications are- insulin glargine, U-500 regular insulin and pramlinitide. With this treatment regimen, while her HDL is still below the normal value it is moving up in the right direction and her liver enzymes as well as LDL values that were high during the previous visits have become normal.

## Conflict of Interest Statement

MCS reports no conflict of interest. AN, has been a speaker Amylin, maker of Symlin (pramlinitide), four times during the past year and has been a speaker for past five years for Sinofi-Aventis, maker of Lantus, and currently makes three presentations per year.

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