Can J Diabetes 38 (2014) 269–272

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Original Research

Once-Weekly Exenatide as Adjunct Treatment of Type 1 Diabetes Mellitus in Patients Receiving Continuous Subcutaneous Insulin Infusion Therapy

Andrea N. Traina PharmD [a], Melinda E. Lull PhD [a,b,*], Adrian C. Hui PharmD, BCPS [d], Toni M. Zahorian PharmD [e], Jane Lyons-Patterson ANP, CDE [c]

[a] AstraZeneca LP, Fort Washington, Pennsylvania, USA
[b] St. John Fisher College, Wegmans School of Pharmacy, Rochester, USA
[c] Rochester General Health System, Rochester, USA
[d] MedStar Union Memorial Hospital, Baltimore, USA
[e] Boston Medical Center, Boston, USA

ARTICLE INFO

Article history:
Received 15 August 2013
Received in revised form
18 October 2013
Accepted 23 October 2013

Keywords:
exenatide
diabetes
glucagon-like peptide-1
incretin

ABSTRACT

Objective: The use of once-weekly exenatide in type 2 diabetes mellitus is well supported, but little is known about its effectiveness in type 1 diabetes. The objective of this study was to determine the clinical efficacy of once-weekly exenatide on glycemic control in patients with type 1 diabetes when added to basal-bolus insulin therapy.
Methods: For this retrospective study, patients with type 1 diabetes, aged 18 years and older, receiving continuous subcutaneous insulin infusion, using a continuous glucose monitoring device or regularly measuring blood glucose levels and receiving 2 mg of exenatide once weekly for at least 3 months were included. Demographic information, glycated hemoglobin (A1C), body weight, body mass index, systolic and diastolic blood pressures, total daily insulin dose, basal and bolus insulin doses, 28-day continuous subcutaneous insulin infusion glucose average and incidence of hypoglycemia were collected at baseline and 3 months after beginning therapy with once-weekly exenatide.
Results: An electronic medical record search identified 11 patients with type 1 diabetes who met the inclusion criteria. Comparing baseline and 3 months after initiation of once-weekly exenatide revealed reductions of 0.6% in A1C ($p=0.013$), 3.7% in body weight ($p=0.008$), 1.7 kg/m^2 in body mass index ($p=0.003$), 13% in total daily insulin dose ($p=0.011$) and 9.3 units in bolus insulin dose ($p=0.015$).
Conclusions: This study revealed that the addition of once-weekly exenatide to insulin therapy for type 1 diabetes patients leads to significant improvements in A1C, body weight, body mass index and insulin doses.

Mots clés :
exénatide
diabète
GLP-1 (*glucagon-like peptide-1*)
incrétine

RÉSUMÉ

Objectif : L'utilisation de l'exénatide une fois par semaine pour traiter le diabète de type 2 est bien approuvée, mais on en connaît peu sur son efficacité pour traiter le diabète de type 1. L'objectif de cette étude était de déterminer l'efficacité clinique de l'exénatide une fois par semaine sur la régulation glycémique des patients atteints de diabète de type 1 lorsqu'il est ajouté à l'insulinothérapie selon le schéma basal-bolus.
Méthodes : Dans cette étude rétrospective, les patients atteints du diabète de type 1 de 18 ans et plus, qui reçoivent une perfusion sous-cutanée continue d'insuline, utilisent un dispositif de surveillance de la glycémie en continu ou mesurent régulièrement les concentrations de glycémie, et reçoivent 2 mg d'exénatide une fois par semaine durant au moins 3 mois ont été inclus. L'information démographique, l'hémoglobine glyquée (A1c), le poids corporel, l'indice de masse corporelle, les pressions artérielles systolique et diastolique, la dose totale quotidienne d'insuline, les doses d'insuline selon un schéma basal et bolus, la moyenne glycémique de la perfusion sous-cutanée continue d'insuline durant 28 jours et la

* Address for correspondence: Melinda E. Lull, PhD, Assistant Professor of Pharmaceutical Sciences, St. John Fisher College, Wegmans School of Pharmacy, 3690 East Avenue, Rochester, New York 14618, USA.
E-mail address: mlull@sjfc.edu

1499-2671/$ – see front matter © 2014 Canadian Diabetes Association
http://dx.doi.org/10.1016/j.jcjd.2013.10.006

fréquence de l'hypoglycémie ont été recueillis au début et 3 mois après le début du traitement par exénatide une fois par semaine.
Résultats : Une recherche dans les dossiers médicaux électroniques a permis de relever 11 patients atteints de diabète de type 1 qui répondaient aux critères d'inclusion. La comparaison au début et 3 mois après le début de l'exénatide une fois par semaine a révélé des réductions de l'A1c de 0,6 % ($p = 0,013$), du poids corporel de 3,7 % ($p = 0,008$), de l'indice de masse corporelle de 1,7 kg/m^2 ($p = 0,003$), de la dose totale quotidienne d'insuline de 13 % ($p = 0,011$) et de la dose d'insuline selon un schéma bolus de 9,3 unités ($p = 0,015$).
Conclusions : Cette étude a révélé que l'ajout de l'exénatide une fois par semaine à l'insulinothérapie pour traiter les patients atteints de diabète de type 1 améliore considérablement l'A1c, le poids corporel, l'indice de masse corporelle et les doses d'insuline.

Introduction

The control of glucose homeostasis in patients with type 1 diabetes is difficult as their beta-cell function is negligible. The deficiency in generating insulin or amylin in these patients leads to an inability to naturally compensate for their variable physiological insulin requirements and suppress postprandial glucagon. Their exogenous insulin boluses injected may not match their dosage requirements and bioavailability. Furthermore, in the near absence of insulin and amylin secretion by beta cells, the physiological postprandial inhibition of glucagon secretion by alpha cells likely does not occur in patients with type 1 diabetes, leading to hyperglucagonemia (1,2). Currently, there are limited data available regarding postprandial glucagon secretion and incretin pathophysiology in patients with type 1 diabetes (1,3). It is essential that this area be investigated further as the erratic and often uncontrollable patterns of glucose concentrations in these patients may be due to hyperglucagonemia (1,2).

Clinically, there is a well-established role for the use of incretin mimetics in patients with type 2 diabetes. However, it is only recently that small studies have begun exploring the role of glucagon-like peptide-1 (GLP-1) agonists in patients with type 1 diabetes. Dupré et al (3) showed that activation of the GLP-1 receptor improves postprandial hyperglycemia in patients with type 1 diabetes, possibly through the suppression of glucagon secretion. Similarly, Raman et al (4) demonstrated a reduction in postprandial glucose after a single twice-daily exenatide injection in adolescents with type 1 diabetes. Kielgast et al (5) demonstrated that a month of treatment with liraglutide (titrated up to 1.2 mg daily after 1 week of 0.6 mg daily) reduced insulin doses without a negative impact on overall glycemic control in patient with type 1 diabetes. Most recently, Varanasi et al (6) showed improved glucose concentrations and less glycemic excursions in adults with type 1 diabetes within 1 week of starting liraglutide 0.6 mg daily.

The aim of our study was to determine the clinical effects of once-weekly exenatide as add-on therapy to insulin in patients with type 1 diabetes. In addition to enhanced glycemic control, we hypothesized that the administration of once-weekly exenatide would lead to improvements in other markers of diabetes management, such as blood pressure and body weight.

Methods

This retrospective observational study was conducted at an ambulatory care endocrinology office affiliated with the Rochester General Health System located in Rochester, New York. After obtaining appropriate protocol approval from the Institutional Review Boards at both Rochester General Health System and St. John Fisher College, subjects were identified, and all pertinent information was gathered utilizing an electronic medical record system search. Patients with type 1 diabetes aged 18 years and older, who were receiving continuous subcutaneous insulin infusion (CSII) and using a continuous glucose monitoring system (CGMS) device or regularly (at least 3 times daily) measuring their blood glucose levels, and who received 2 mg of exenatide once weekly for at least 3 months were included. Patients were excluded if they had been diagnosed with type 1 diabetes for less than 6 months, had lack of documented C-peptides or glutamic acid decarboxylase (GAD) antibodies or documented detectable C-peptides or negative GAD antibodies, use of once-weekly exenatide for less than 3 months or a lack of follow-up data.

For patient records meeting all study criteria, data were collected at the initiation of once-weekly exenatide (baseline) and 3 months after once-weekly exenatide initiation. Data collection included demographic information (age, gender, ethnicity, height, duration of type 1 diabetes, C-peptide and GAD antibody levels) and the following medical information: body weight (in kg) using a calibrated in-office scale, body mass index (BMI), glycated hemoglobin (A1C) obtained from one of the Rochester General Health System laboratories, blood pressure (BP) measured manually by office nurses, total daily insulin dose (TDD), basal and bolus insulin doses (in number of units and as a percentage of TDD [data obtained from 28-day Carelink upload at baseline and 3-month follow-up appointment]), CSII blood glucose average over 28 days and hypoglycemia incidence over 28 days (obtained from 28-day Carelink upload as above). Hypoglycemia was defined as a documented blood glucose of <3.9 mmol/L.

Statistical analysis

Differences in each variable were determined using a paired *t* test and SigmaPlot 11.0 software (SyStat Software, San Jose, CA) and expressed as mean ± SD. Changes were considered statistically significant with a p value of less than 0.05. Body weight and TDD were each expressed as a percentage of baseline, as baseline values for individual patients were highly variable.

Results

The electronic medical record search identified 101 patients receiving once-weekly exenatide therapy. Of these, 29 patients had type 1 diabetes, and the remaining 72 patients had type 2 diabetes. Eleven of the 29 patients with type 1 diabetes met the remaining study criteria. The average duration of follow up was 90±8 days, mean age was 53±11.1 years, average duration of diabetes was 39 years (range 11 to 49 years), median age at diagnosis was 17 years (range 2 to 54 years), 4 patients used a CGM device, 8 patients were female and all 11 were Caucasian. All patients had documented negative (<0.1 ng/mL) C-peptide and positive (>5 IU/mL) GAD antibody levels.

Eighteen of the 29 patients with type 1 diabetes did not meet the inclusion criteria owing to either multiple daily insulin injections (n=2), never having started treatment with