

Real World Clinical Experience with exenatide, a long term study on weight and A1c control

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Abstract

We evaluated the sustained efficacy of exenatide added to oral anti-diabetic therapy in patients who were either insulin naïve (group A, n=132) or insulin requiring (group B, n=109). A single physician in a private practice endocrinology office made the clinical decision to add exenatide as needed to improve A1c to a target less than 6.5%. Baseline therapies were composed of combinations of metformin, pioglitazone, sulfonylurea and insulin. All patients were titrated from 5 to 10mcg SQ of exenatide BID as tolerated and all sulfonylureas were discontinued. In group A, exenatide was the only injectable agent used during the follow-up period. Measurements of weight, BMI, A1C, blood pressure, lipids, and medication utilization were assessed every 3 months for a maximum of 21 months after initiation of exenatide. Group A patients had a mean duration of diabetes of 7.9 ±0.7 yr (±SD) and a mean A1c of 7.1±1.9%. Group B patients had a mean duration of diabetes of 15.4 ±0.9 yr and a mean A1c of 8.1±0.6%. Mean A1C at 21 months for the non insulin requiring group (n=47) (fig.1) was 6.31% (p= 0.0001), and 7.32% (p= 0.0011) for insulin requiring patients (n=43) (fig.2). Mean weight change was -1.7 kg (p = <0.0001) for Group A (n=51) (fig.1) and -4.3 kg (p = <0.0001) for Group B (n=45) (fig.2). The addition of exenatide to combination oral therapy with or without insulin results in sustained weight loss and improved A1C values with substantial reductions in the total daily dose of insulin for Group B.

Background and Objective

BACKGROUND:

There is a significant knowledge gap regarding long term exenatide use in multi-drug diabetic treatments including insulin. Limited data has been collected to assess the use of exenatide concomitantly with thiazolidinediones. There is limited short term clinical data for use with insulin and no long term data on combination therapy consisting of thiazolidinedione, metformin and insulin.

PRIMARY OBJECTIVE:

To assess the A1C and weight change independently from baseline when adding exenatide in an uncontrolled type 2 diabetes patient population being treated in a real world, clinical practice setting.

Methods and Results

RESEARCH METHODS :

The patient population was taken from a single practitioner's practice. As such, the investigator was not blinded to the treatment combinations chosen. A retrospective chart review of all patients on exenatide was performed at each visit and reported in 3 month intervals. The final data point is 33 months post initiation of exenatide. Medical staff employed in the office collected data into spreadsheets removing any identifying information. This data was assessed statistically utilizing a student paired t-test. The patients were divided into 2 groups based on insulin users (109 patients) and non-insulin users (132 patients). All patients continued on their usual combination oral therapy with the exception that sulfonylureas were discontinued. Insulin using patients were given titration schedules (with insulin doses being reduced by 20 to 50% as exenatide was begun). The visit schedule and monitoring for the patients was governed by current clinical practice guidelines and at the discretion of the practitioner. All current practice guidelines as set by AACE, NCEP and ADA were followed and maintained. IRB approval was not required due to the practitioner's HIPPA form listing chart review for research purposes as a specific consent the patient gives upon entry in to the practice.

fig. 1: Group A (non-insulin users)

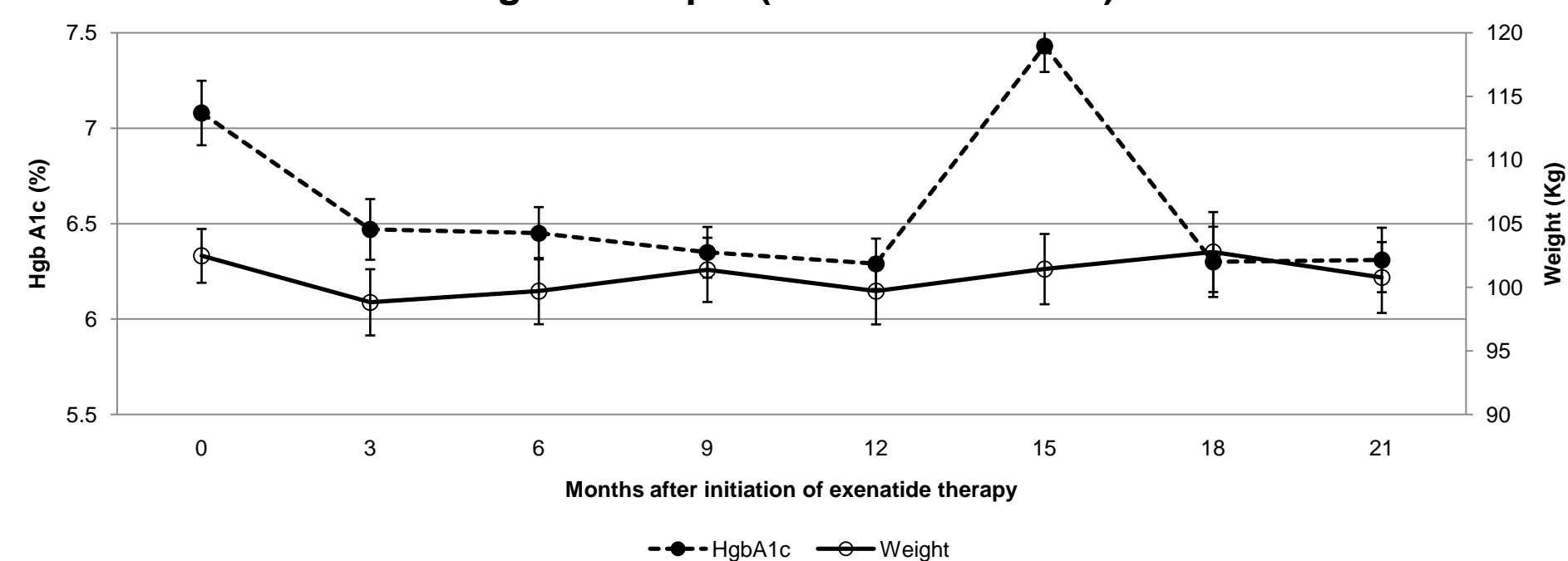
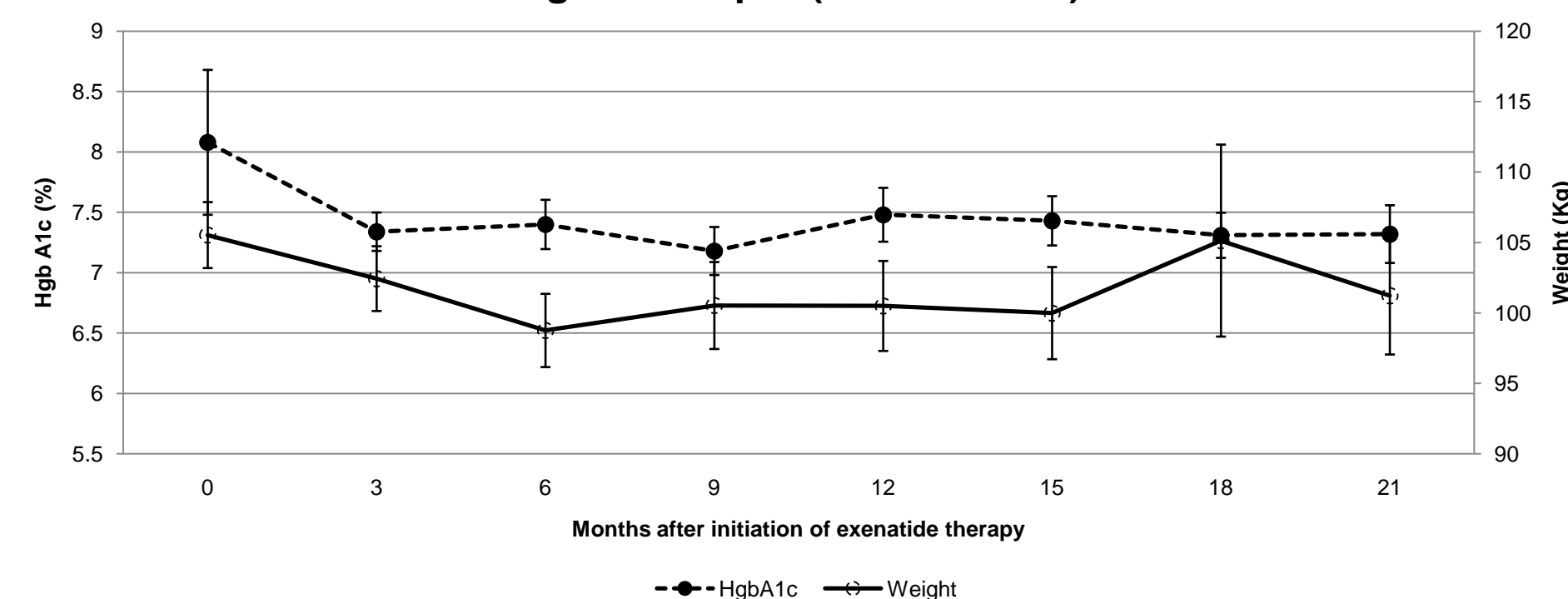


fig. 2: Group B (insulin users)



Conclusions

The addition of exenatide improved HbA1c with minimal weight change in either group. The longer mean duration of diabetes in the insulin using group is consistent with a greater degree of insulin deficiency. Conventional wisdom might have suggested that insulin requiring patients would not have responded as robustly to exenatide as more recently diagnosed patients with diabetes. The final A1C of the non-insulin users is nearly unprecedented and occurred in the face of very limited hypoglycemia (data not formally presented). No patients had significant adverse events or hospitalizations for hypoglycemia. This lack of hypoglycemia was anticipated for the non-insulin using group, and comforting for the insulin users. All of these changes are consistent with previous short-term and long-term trials evaluating the use of exenatide in the setting of oral and insulin therapies. These results support the position of initiating exenatide after oral therapy rather than proceeding to the addition of insulin (and coincident discontinuance of agents that previously induced reductions in HbA1c - as called for in the ADA/EASD consensus algorithm). The improvements achieved in the insulin user also suggest that this is a viable add on therapy with little or no weight gain (favoring improved cardiometabolic profile). One limitation of our data set is that it spans only 21 months. On the other hand, most clinical trials are much shorter. One major strength of this clinical outcomes investigation is that it represents what can be accomplished in a real-world clinic environment as opposed to the controlled atmosphere of a clinical trial.

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