LIRAGLUTIDE IMPROVES BETA-CELL FUNCTION, MEASURED BY THE C-PEPTIDE/GLUCOSE RATIO, IN OBESE PATIENTS WITH TYPE 2 DIABETES.

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INTRODUCTION

Beta-cell function declines progressively in patients with type 2 diabetes (T2D). the fasting C-peptide/glucose ratio (Cp/G) is used for its evaluation. The GLP-1 receptor agonist liraglutide improves glucose and weight control, presumably due to improvement of beta-cell function and/or mass. This study evaluates the effect of a 6-months' treatment with liraglutide in beta-cell function, measured by Cp/G, in patients with obesity and T2D.

PATIENTS AND METHODS

We performed an observational retrospective and prospective analysis of a cohort of 43 patients (24 women) with orally-treated T2D and obesity, to whom liraglutide 1.2 mg/day was added. At 3 months, dosage of liraglutide was increased to 1.8 mg/day in those cases in which HbA1c or weight goals were not fully achieved. We evaluated clinical and analytical data before and after 6 months of treatment. Statistical analysis with IBM SPSS Statistics Inc., version 21.0, using Cp/G as a surrogate marker of beta-cell function.

RESULTS

Patients' basal characteristics prior to initiating liraglutide are shown in **table 1**. Mean T2D duration was 6.7 ± 3.8 years. Twenty six (60.5%) patients previously received one oral hypoglycemic agent (OHA) (metformin), and the rest of them were on two OHA. At 3 months, dosage was increased to 1.8 mg/day in 24 (55.8%) cases; these patients had higher pre-treatment HbA1c levels (7.8 ± 0.9 vs 7.3 ± 0.7%, p=0.025) and lower Cp/G values (0.0235 ± 0.0099 vs 0.0295 ± 0.0101, p=0.057), in comparison to those who remained on 1.2 mg/day.

After 6 months of liraglutide, percentage weight loss (%WL) was 5.2 ± 4.8 kg. BMI, FG, HOMA and HbA1c were significantly decreased (**table 1**). Mean HbA1c reduction was -0.79 ± 0,92% (which meant a reduction of 10.6 ± 11.5%). cP/G values at 6 months increased 15.4 ± 36.6%, reaching 0.0296 ± 0.0148. Amelioration occurred regardless of pretreatment HbA1c or final dose of liraglutide.

Basal cP/G values correlated with %WL and HbA1c at 6 months (**figure 1**). Decrease of HbA1c levels and %WL were similar regardless of pre-treatment HbA1c, BMI or Cp/G (**figures 2-4**).

Patients who were previously on only one OHA showed higher Cp/G at 6 months (0.0341 vs 0.0226, p<0.05) (**figure 5**). Individuals with pre-treatment Cp/G within the lower quartile achieved 6-month HbA1c levels < 7% less frequently (**figure 6**). Patients to whom liraglutide was increased to 1.8 mg/day achieved lower %WL (7.1 ± 5.7 vs 3.6 ± 3.1, p=0.013) (**figure 7**), but there were no differences in the variation of HbA1c or Cp/G values.

ANTHROPOMETRIC AND ANALYTICAL DATA	Pre-liraglutide (mean ± SD)	6 months after liraglutide (mean ± SD)	*p*
BMI (kg/m²)	39.3 ±4.9	37.3 ± 5.2	0.000
Fasting glucose (mg/dL)	149.8 ± 36.9	132.5 ± 47.3	0.006
HbA1c (%)	7.6 ± 0.8	6.8 ± 1.2	0.000
HOMA-IR	6.1 ± 3.3	4.8 ± 3.2	0.019
C-peptide/glucose	0.0261 ± 0.0103	0.0296 ± 0.0148	0.047

Table 1. Anthropometric and analytical data, before and after 6 months of treatment with liraglutide. T-test for paired samples.

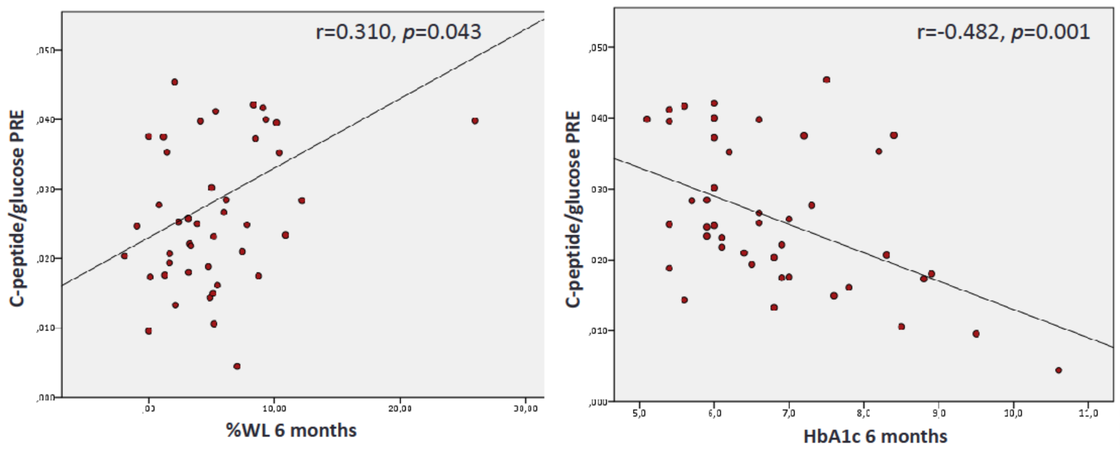

Figure 1. Bivariate correlations (Pearson)

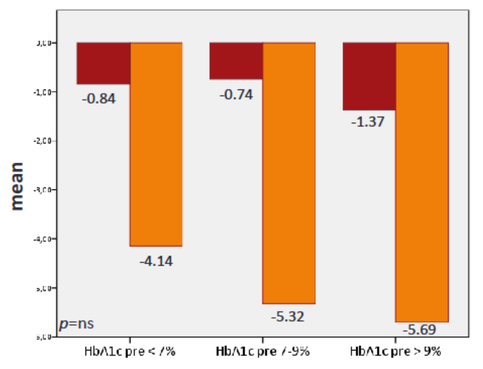

Figure 2. HbA1c reduction (simple difference) ■ and %WL ■, according to pre-treatment HbA1c.

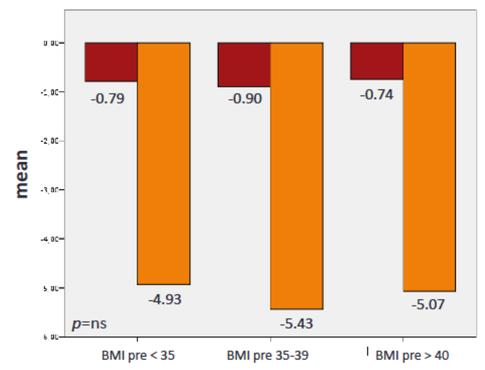

Figure 3. HbA1c reduction (simple difference) ■ and %WL ■, according to pre-treatment BMI

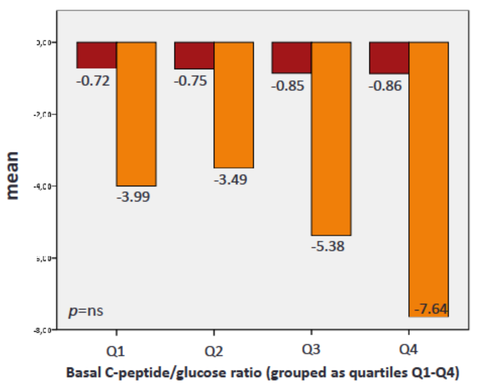

Figure 4. HbA1c reduction (simple difference) ■ and %WL ■, according to pre-treatment C-peptide/glucose ratio, grouped as quartiles.

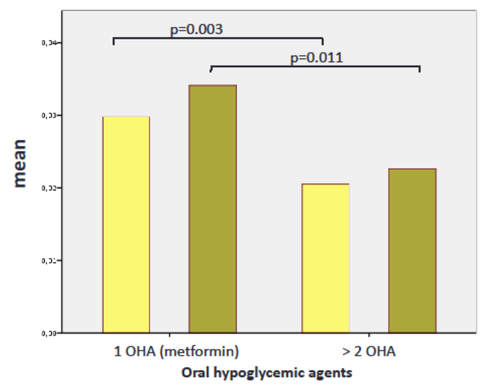

Figure 5. C-peptide/glucose ratio before ■ and after 6 months of liraglutide ■, according to previous hypoglycemic treatment with oral agents.

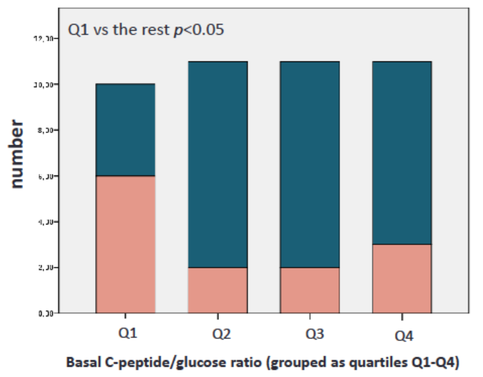

Figure 6. Number of patients with HbA1c values at 6 months < 7% ■ and > 7% ■, according to pre-treatment C-peptide/glucose ratio, grouped as quartiles.

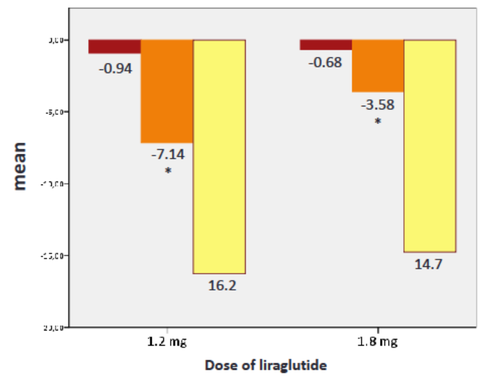

Figure 7. HbA1c reduction ■, %WL ■ and porcentual difference in C-peptide/glucose ratio ■, according to liraglutide dose

CONCLUSIONS

Liraglutide seems to improve beta-cell function, measured by Cp/G, after 6 months, regardless of pre-treatment BMI, HbA1c or Cp/G. A lower basal pre-treatment Cp/G is associated to lower rates of optimal glucose metabolism control after 6 months of treatment with GLP-1 agonists.

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Diabetes (complications & therapy)

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