LACK OF GLUCAGON EFFECT OF GLP-1 RECEPTOR AGONISTS: ASSESSMENT DURING A MIXED MEAL TOLERANCE TEST

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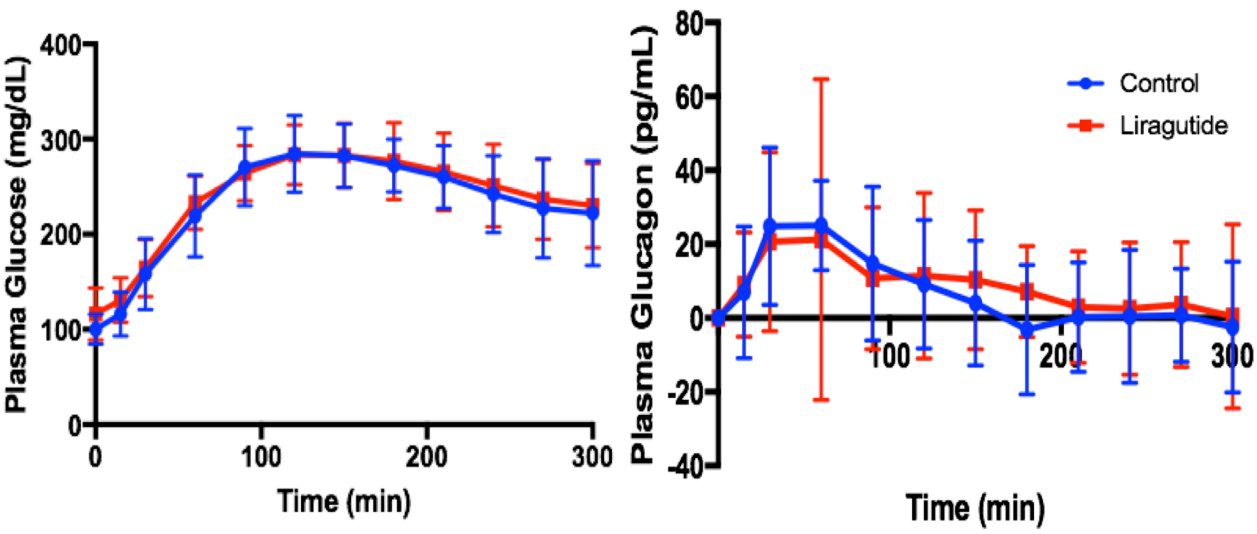
Background: Postprandial hyperglycemia remains challenging in type 1 diabetes (T1D) due, in part, to dysregulated glucagon secretion. While acute GLP-1 receptor agonist infusion studies suggested suppressed glucagon after mixed-meal feeding in T1D, more recent GLP1 treatment studies demonstrate conflicting results.

Objective: In this study, mixed-meal tolerance tests (MMTT) explored how the GLP1 receptor agonist, liraglutide, effects meal-stimulated excursions in plasma glucose (PG) and glucagon in patients with T1D.

Methods: Subjects underwent two MMTTs, before and after treatment with liraglutide (1.8mg/day) and insulin adjusted, as needed.
The MMTTs utilized Boost High Protein Energy Drink. PG and glucagon were measured for 5-hrs. Normal fasting PG levels were achieved by overnight closed-loop insulin delivery.



Results: We enrolled 11 participants (aged23±3y, HbA_{1C}7.6±0.9%). Plasma glucose and glucagon were nearly identical in both studies at baseline and following Boost ingestion (see *Figure*). The mean plasma glucagon AUC observed during the control study was not suppressed after treatment with liraglutide (control: 2352±997 vs. lira: 2705±1473 pg/ml*min, p=ns). Despite the short duration of treatment, there was a reduction in both body weight (4.8±2.4%, p=0.001) and insulin dose (~25%, p=0.001) with liraglutide.

Conclusion: Plasma glucagon response to MMTT in T1D is not suppressed after 3-4-wks of treatment with liraglutide. This suggests that the benefits of liraglutide as an adjunctive treatment for T1D could be mediated by its effects on satiety, leading to weight loss and reductions in insulin requirements.

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