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ORIGINAL ARTICLE

Effect of the GLP-1 analog liraglutide on satiation and gastric sensorimotor function during nutrient-drink ingestion

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BACKGROUND/AIM: Liraglutide, a glucagon-like peptide-1 analog, induces weight loss. We investigated whether liraglutide affects gastric accommodation and satiation by measuring the intragastric pressure (IGP) during nutrient-drink consumption and using the barostat technique.

METHODS: Ten healthy volunteers (HVs) were tested after placebo, 0.3, 0.6 or 1.2 mg liraglutide administration. IGP was studied during intragastric nutrient-drink (1.5 kcal ml^{-1}) infusion (60 ml min^{-1}), while the HVs scored their satiation on a graded scale until maximal satiation. In a separate session, isobaric distentions were performed using the barostat with stepwise increments of 2 mm Hg starting from minimal distending pressure, although HVs scored their perception; gastric volume was monitored 30 min before and until 60 min after ingestion of 200 ml of nutrient drink. Data are presented as mean ± s.e.m. comparisons were performed with ANOVA ($P<0.05$ was significant).

RESULTS: During nutrient-drink infusion, IGP decreased with 4.1 ± 0.7, 3.0 ± 0.4, 2.1 ± 0.3 and 2.6 ± 0.4 mm Hg (placebo, 0.3, 0.6 and 1.2 mg liraglutide, respectively; $P<0.05$). The maximum-tolerated volume was not different, except after treatment with 1.2 mg liraglutide (695 ± 135 ml) compared with placebo (1008 ± 197 ml; $P<0.05$); however, 1.2 mg liraglutide induced nausea in all volunteers. In the barostat study, liraglutide did not affect the perception or compliance, but significantly decreased gastric accommodation to the meal (168 ± 27 vs 78.8 ± 36.4 ml after treatment with placebo and 0.6 mg liraglutide, respectively; $P<0.05$).

CONCLUSION: Although no effect on perception, compliance or satiation was observed, liraglutide inhibited gastric accommodation. Whether this effect is involved in the anorectic effect of liraglutide remains to be determined.

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Keywords: GLP-1; liraglutide; gastric accommodation; satiation; intragastric pressure

INTRODUCTION

Food intake can be regulated via satiety signals from the gut that directly influence the brain centers, as the hypothalamus and the brainstem.[1–4] These signals include circulating levels of orexigenic and anorexigenic gut peptides, and neural signals through vagal afferents.[2] The stomach has a central role in the regulation of food intake. During food intake, the muscles of the stomach relax, so that the intragastric pressure (IGP) does not increase despite the large volumes of food we sometimes consume. This reflex relaxation, also referred to as gastric accommodation, is believed to have a role in the regulation of food intake. Indeed, we previously showed that food intake is decreased in functional dyspeptic patients with impaired gastric accommodation.[3]

Glucagon-like peptide-1 (GLP-1) is a gastrointestinal regulatory peptide secreted from the mucosal endocrine L cells in response to the nutrient ingestion.[4] GLP-1 acts mainly as incretin, enhancing glucose-stimulated insulin secretion and glucose homeostasis.[4] In addition, GLP-1 acts as an anorexigenic peptide, decreasing hunger feelings. In animal models, intracerebroventricular injection of GLP-1 inhibits food intake, and intravenous infusion decreased food intake in normal weight and obese humans.[5,6] GLP-1 reduces postprandial glycemia, not only through its hormonal effects, but also by its effects on gastrointestinal motility. GLP-1 is a mediator of the ileal brake,[7] and administration of liraglutide (a GLP-1 mimetic) has been shown to slow solid and liquid gastric emptying, reduce gut motility, inhibit antro-pyloro-duodenal motility, and enhance gastric accommodation.[8–15]

As native GLP-1 has a short elimination half-life of 1–2 min, because of rapid metabolism by the widely distributed enzymes dipeptidyl peptidase-IV and neutral endopeptidase 24.11,[16] one method currently being pursued for the therapeutic targeting of GLP-1 receptors is the production of GLP-1 analogs that are resistant to degradation by dipeptidyl peptidase-IV and neutral endopeptidase 24.11.

Liraglutide is a GLP-1 analog with an additional 16-carbon fatty acid and a small amino-acid-based spacer, which confers reversible binding of the agonist to albumin and increases resistance to dipeptidyl peptidase-IV activity, providing liraglutide with a half-life of ~13 h.[17] Although *in vitro* studies suggest that liraglutide binds to GLP-1 receptors with similar potency as native GLP-1,[17] clinical data indicate that the spectrum and magnitude of actions of GLP-1 and liraglutide are not identical. These differences may be attributed to differences in concentrations, but potentially also to different binding profiles.[18] Several studies have shown that daily administration of liraglutide (1.8 mg per day) is associated with decreased food intake and weight loss.[19–22] The mechanism underlying weight loss with liraglutide treatment remains to be elucidated although delay in gastric emptying, early satiation and decreased sense of appetite have all been suggested.[2]

The aim of this study was to investigate the influence of a single treatment with liraglutide on gastric sensorimotor function and meal-induced satiation in humans that could help to elucidate its effect on food intake further. We measured the effects of liraglutide on IGP during intragastric nutrient infusion and on the

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compliance and relaxation of the proximal stomach during a barostat study.

MATERIALS AND METHODS

Overall design

Our evaluation of the effects of liraglutide consisted of two study protocols. First, a double-blind randomized placebo-controlled study of the effect of three different doses of liraglutide on IGP during nutrient infusion and nutrient tolerance was performed. Second, a single effective liraglutide dose was selected based on the IGP monitoring study, for evaluation in a double-blind randomized placebo-controlled study of the effect of liraglutide of gastric sensorimotor function assessed by the barostat.

Study subjects

Ten Healthy volunteers (HVs; seven men, age 33.3 ± 9.7 years, body mass index 23.2 ± 2.2 kg m^{-2}) participated in the study. All study procedures were approved by the Ethics Committee of the Leuven University Hospital, Belgium. All participants gave written, informed consent. Exclusion criteria included the presence of symptoms or a history of gastrointestinal diseases, diabetes, any other significant disease or psychological disorder. Moreover, as liraglutide could decrease the blood glucose concentrations, we especially excluded volunteers that suffered from hypoglycemia or took any drugs that are known to decrease blood glucose concentration. HVs came to the motility unit after at least 6-h fasting. HVs were asked to refrain from alcohol, tea and coffee, at least 12 h before participation, moreover, they were asked to refrain from smoking cigarettes, at least 1 h before the start of the experiment.

Treatments

Liraglutide (Victoza, Novo Nordisk, Belgium; 0.3, 0.6 and 1.2 mg) was administered as an abdominal subcutaneous injection 12–20 h before the start of each experiment, hence on the day preceding the experiment.[23] A washout period of at least 1 week was observed between treatments, and the order of the respective treatments was determined at random. For the placebo arm of the study, we used saline (subcutaneous injection in the abdomen).

IGP measurement during intragastric nutrient-drink infusion

IGP was assessed using a high-resolution solid-state manometry system (36 channels, 1 cm in between each channel, Manoscan 360; Sierra Scientific Instruments, Los Angeles, CA, USA; Manoview analysis software v2.0.1). Upon arrival in the clinic, the manometer was positioned through the nose so that at least one sensor was located in the lower esophageal sphincter (lower esophageal sphincter (LES), detected as a clearly elevated pressure zone compared with oral and aboral areas), although IGP was measured using the average pressure of the first five pressure channels that were clearly positioned below the LES or the pressure area influenced by the LES (~3–8 cm under the LES, as determined from the high-resolution plot).[24] An infusion catheter (Flocare; Nutricia, Bornem, Belgium) was positioned in the stomach through the mouth. The tip of the infusion catheter was positioned ~5 cm under the LES, and its position was verified by fluoroscopy. From preliminary experiments, we know that the position of the infusion catheter does not affect the IGP during intragastric nutrient-drink infusion.[24]

After positioning the catheters, and after a stabilization period of at least 30 min, intragastric infusion of a nutrient drink (Nutridrink, Nutricia; 630 kJ, 6g proteins, 18.4g carbohydrates and 5.8g lipids per 100 ml) started at a constant speed of 60 ml min^{-1} (determined by an automated system using a peristaltic pump).[24] At 1-min intervals, the subjects were asked to score their satiation using a graphic rating scale that combined verbal descriptors on a scale graded from 0–5 (1, threshold; 5, maximum satiety). In addition, at 5-min intervals, the HVs were asked to fill out a visual analog scale (VAS) for seven epigastric symptoms (fullness, nausea, bloating, belching, epigastric pain, satiety and abdominal cramps). Intragastric infusion was stopped as soon as the volunteers scored maximal satiation. Ten minutes thereafter, the catheters were disconnected and removed and the volunteers could leave the unit.

Sensitivity to gastric distention and gastric accommodation assessed with a barostat

Based on the IGP experiments, we selected the 0.6 mg liraglutide dose for further investigations with the barostat. Sensitivity to gastric distention and gastric accommodation to a meal were studied using a gastric barostat, as previously described.[25] Upon arrival in the clinic, a double-lumen polyvinyl tube (Salem sump tube 14Ch; Sherwood Medical, Petit-Rechain, Belgium), with an adherent plastic bag (1200 ml capacity; 17 cm maximal diameter) finely folded, was introduced through the mouth and secured to the subject's chin with adhesive tape. The position of the bag was checked fluoroscopically. The polyvinyl tube was then connected to a programmable barostat device (Synectics Visceral Stimulator, Stockholm, Sweden). To unfold the bag, it was inflated with a fixed volume of 300 ml of air for 2 min with the study subject in a recumbent position, and again deflated. Subjects were then positioned in a comfortable sitting position with knees bent (80°) and trunk upright in a specifically designed bed.

After a 30-min adaptation period, minimal distending pressure (MDP) was first determined by increasing the intrabag pressure by 1 mm Hg, every 3 min, until a volume of 30 ml or more was reached.[26] This pressure level equilibrates the intraabdominal pressure. Subsequently, isobaric distentions were performed in stepwise increments of 2 mm Hg, starting from MDP, each lasting 2 min, while the corresponding intragastric volume was recorded. Subjects were instructed to score their perception of upper abdominal sensations at the end of every distending step, using a graphic rating scale that combined verbal descriptors on a scale graded 0–6. In addition, we evaluated the intensity of nine upper abdominal symptoms (discomfort, fullness, nausea, bloating, heartburn, belching, epigastric pain, satiety and abdominal cramps) using a 10-cm VAS scoring system. The end point of each distension sequence was established at an intrabag volume of 1000 ml or when the subject reported discomfort or pain (score 5 or 6).

After a 30-min adaptation period with the bag completely deflated, the pressure level was set at MDP + 2 mm Hg for at least 90 min. After 30 min, a liquid meal (200 ml, 300 kcal, 13% proteins, 48% carbohydrates, 39% lipids; Nutridrink, Nutricia) was administered. Gastric tone measurement was continued for 60 min after the meal. At 5-min intervals, VAS scores were completed to evaluate the intensity of nine abdominal symptoms. Hereafter, the balloon was retracted and the volunteers could leave the hospital.

Data analysis

The study was designed to have an 80% power to detect 30% differences in IGP drop during the nutrient challenge test, and a 30% decrease in gastric accommodation measurement during the barostat studies.

IGP. The original data were imported from the recording software to Microsoft Excel (Microsoft, USA). We were primarily interested in slow IGP changes that could reflect changes in the gastric muscle tone. Therefore, in order to avoid the influence from movement artifacts and artifacts caused by coughing, sneezing, moving or swallowing, a moving median was calculated per channel from the original data (median value over 1 min of original data). Per channel, a baseline value was calculated from the moving median data as the average pressure in the last 5 min of the stabilization period. Data were presented per minute as the difference of the minimum moving median value in that minute and the baseline value. Data were presented as mean ± s.e.m. and compared with a two-way analysis of variance (ANOVA) ($P<0.05$ was considered significant).

Barostat. The perception threshold was defined as the first level of the intraballoon pressure (during stepwise ramp distentions) and the corresponding volume that evoked a perception score of 1 or more. The discomfort threshold was defined as the first level of the intraballoon pressure and corresponding volume that provoked a perception score of 5 or more.[25] Pressure thresholds were expressed as pressures relative to MDP. Based on previous studies, gastric compliance was calculated as the slope of the pressure–volume curve obtained by stepwise ramp distentions (ml mm Hg^{-1}).[25] Similarly, pressure–perception curves were obtained from the stepwise distentions. Comparisons were performed using a *t*-test and mixed-model analysis for the accommodation data. Data are presented as mean ± s.e.m. ($P<0.05$ was significant).

During the evaluation of meal-induced fundic relaxation at MDP + 2 mm Hg, the mean intraballoon volume was calculated over consecutive 5-min intervals. To assess the effect of liraglutide on gastric accommodation, gastric relaxation was quantified as the difference between the average volume during the 60 min after the meal and the last 10 min preprandially. In addition, the area under the curve (AUC) of the accommodation measurement was compared using a paired Student's *t*-test. For each symptom evaluated during barostat studies and meal-induced satiety testing, the cumulative symptom score was obtained by adding scores at

each individual time point and expressed as area under the curve. The symptom scores were compared using Student's *t*-test.

RESULTS

Conduct of the study

After nausea and nocturnal vomiting had occurred in the first five volunteers in the IGP study after one of the study drug administrations, randomization code was broken, revealing that this occurred after the highest dose tested (1.2 mg). This dose was therefore eliminated for all subsequent volunteers and the 0.6 mg dose was chosen for the barostat studies.

In the IGP measurement studies, 10 subjects received placebo or 0.3 mg liraglutide or 0.6 mg liraglutide; only 5 subjects received the 1.2 mg dose. In the barostat studies, 10 subjects received placebo and 0.6 mg liraglutide.

Manometry

IGP during nutrient infusion. The dosages of 0.3 and 0.6 mg liraglutide did not affect meal-induced satiation, whereas 1.2 mg tended to increase satiation scores in the 5 subjects receiving this dose ($P = 0.45$; Figure 1). The maximum nutrient volumes tolerated by the volunteers were 912 ± 133, 851 ± 144, 847 ± 116 after placebo, 0.3 and 0.6 mg liraglutide, respectively (Figure 2a). When separately analyzing the maximum-tolerated volume in the 5 subject that received 1.2 mg liraglutide vs placebo, a significant difference could be observed (694 ± 135 vs 1008 ± 197 ml, respectively, $P < 0.05$; Figure 2b).

In all treatment groups, IGP decreased initially during nutrient-drink infusion and gradually increased thereafter (Figure 3a). The average pressure during nutrient-drink infusion was 4.1 ± 0.7, 3.0 ± 0.4, 2.1 ± 0.3 and 2.6 ± 0.4 mm Hg after placebo, 0.3, 0.6 and 1.2 mg liraglutide, respectively (placebo vs 0.6 mg liraglutide $P < 0.05$; Figure 3b).

The pressure-drop during nutrient-drink infusion was 5.5 ± 0.7, 4.9 ± 0.6, 3.8 ± 0.5 and 4.1 ± 0.8 mm Hg after placebo, 0.3, 0.6 and 1.2 mg liraglutide, respectively (Figure3c).

During intragastric nutrient-drink infusion, 0.3 and 0.6 mg liraglutide did not significantly influence VAS scores for any of the seven abdominal symptoms. The dosage of 1.2 mg liraglutide was associated with higher scores for nausea, vomiting, early satiation and decreased appetite scores (Table 1; $P < 0.05$).

Barostat

The MDP did not differ between both study conditions (7.0 ± 0.4 vs 7.7 ± 0.4 mm Hg after placebo and liraglutide 0.6 mg pretreatment, respectively). Liraglutide pretreatment tended to enhance fasting gastric compliance ($P = 0.05$), but the pressure thresholds for first perception or discomfort during gastric distentions, and the corresponding intraballoon volumes, were similar for both study conditions (Table 2).

Preprandial balloon volumes did not differ between both conditions. However, the postprandial volume was lower after liraglutide ($P < 0.0001$; table 2). Gastric accommodation was significantly inhibited by liraglutide (168 ± 27 vs 78.8 ± 36.4 ml, $P < 0.05$; Figure 4). The AUC of the accommodation measurement was significantly lower after liraglutide compared with placebo (4453.1 ± 317.2 vs 3044.5 ± 317.6 ml min, $P = 0.032$).

Liraglutide did not significantly influence the VAS scores for any of the nine epigastric symptoms during the postprandial period or during isobaric pressure distentions (details not shown).

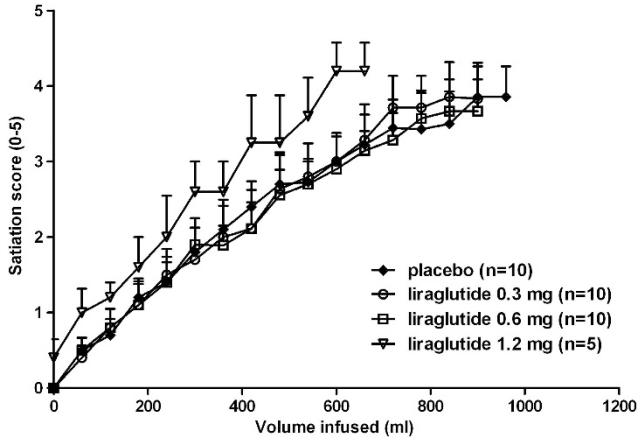

Figure 1. Influence of 0.3, 0.6 and 1.2 mg liraglutide and placebo on meal-induced satiation scores during nutrient-drink infusion. Results presented as mean + s.e.m.

DISCUSSION

In this study, we used two different techniques to demonstrate for the first time that lower range doses of the GLP-1 analog liraglutide inhibit gastric accommodation in man without significantly affecting satiation. The 1.2 mg dose of liraglutide significantly increased satiation, but this is most likely due to the side effects observed with this dose.

Gastric accommodation is a reflex that enhances the storage capacity of the stomach during food intake. Indeed, in between meals, the proximal stomach is characterized by a basal muscle tone, however, during food intake, the muscle tone decreases, a reflex that is mainly mediated via parasympathetic nerves, decreasing the contractile cholinergic input while activating the release of nitric oxide (NO). Gastric accommodation increases the compliance of the stomach muscles and thereby increases the storage capacity of the stomach while keeping IGP low.[27] The gastric barostat is regarded the golden standard to assess gastric accommodation[28] in healthy subjects and dyspeptic patients. However, it should be emphasized that the procedure is invasive, time consuming and uncomfortable, limiting its feasibility in routine clinical practice. In addition, the presence of a gastric

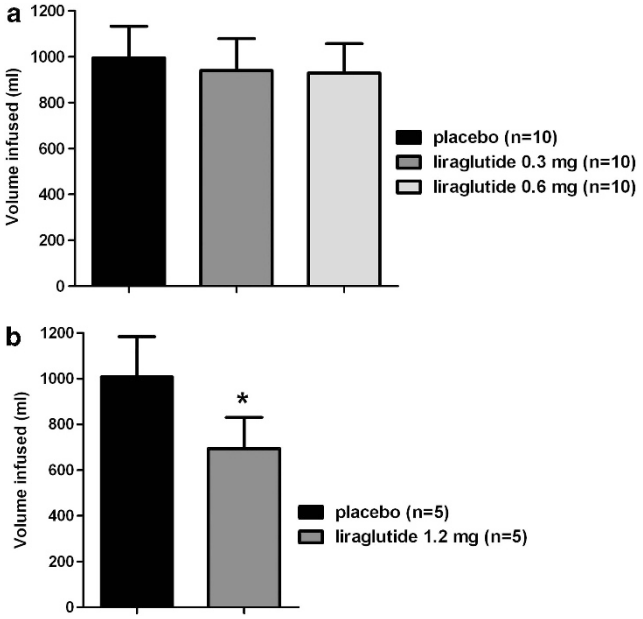

Figure 2. (**a**) Maximum-tolerated volume during intragastric nutrient infusion after placebo, 0.3 mg and 0.6 mg liraglutide treatment. (**b**) Maximum-tolerated volume after placebo and 1.2 mg liraglutide treatment. Results presented as mean + s.e.m.. *$P < 0.05$.

balloon has been shown to interfere with normal gastric physiology, as the direct stimulus imposed by the balloon on the proximal stomach wall may alter intragastric distribution of the meal and may result in exaggeration of antral relaxation.[29] These limitations have served as an impetus to develop various alternative, less invasive diagnostic techniques that assess gastric accommodation.

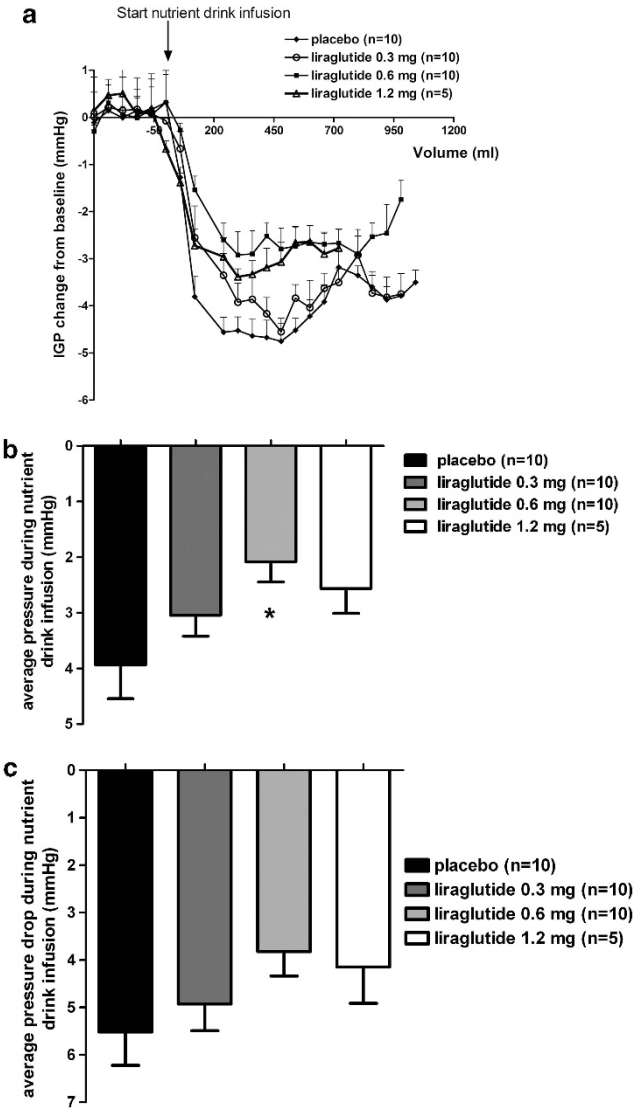

Figure 3. (**a**) Intragastric pressure (IGP) change from baseline pressure during intragastric nutrient-drink infusion. Nutrient drink started at $T=0$ min. (**b**) Average pressure during intragastric nutrient-drink infusion. *$P<0.05$ (**c**) Average pressure drop during intragastric nutrient-drink infusion.

We previously showed that gastric accommodation can be assessed using IGP measurement during intragastric nutrient infusion. This method was perceived as less invasive compared with the barostat, and provides a more physiological alternative for the barostat, especially to assess gastric accommodation during food intake.[24] IGP during nutrient infusion decreases rapidly and gradually recovers upon continuous nutrient infusion, indicating gastric relaxation upon nutrient infusion.[24]

Liraglutide dose dependently decreased the maximum IGP decrease upon nutrient infusion, indicating impaired gastric accommodation. This finding is confirmed using the barostat,

Table 2. Influence of placebo and 0.6 mg liraglutide on gastric compliance, accommodation and perception of gastric distention in 10 healthy volunteers. Data are expressed as percentage (%) of a VAS scale (10 mm = 100%)

	Placebo	*liraglutide*	P-*value*
MDP (mm Hg)	7 ± 0.4	7.7 ± 0.4	$P=0.35$
Gastric compliance premeal (ml mm Hg^{-1})	51.8 ± 10.1	78.6 ± 7	$P=0.05$
Preprandial intraballoon volume (ml)	236.8 ± 24.7	211.6 ± 24.04	$P=0.57$
Postprandial intraballoon volume (ml)	362.9 ± 41.06	274.8 ± 33.9	$P<0.0001$
Perception threshold (mm Hg above MDP)	2 ± 0.42	2 ± 0.37	$P=0.35$
Discomfort threshold (mm Hg)	10.8 ± 0.8	9.6 ± 0.8	$P=0.77$
Volume at first perception (ml)	157.6 ± 17.8	132.6 ± 17.3	$P=0.32$
Volume at discomfort (ml)	588.4 ± 68.3	645.10 ± 45.7	$P=0.50$

Abbreviation: MDP, minimal distending pressure.

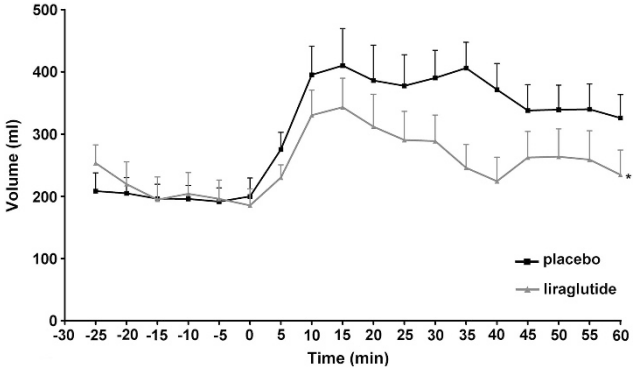

Figure 4. Influence of 0.6 mg liraglutide or saline on intraballoon volumes before and after the meal. Meal-induced relaxation was significantly inhibited by liraglutide. *$P<$ 0.05

Table 1. Influence of placebo and 1.2 mg liraglutide on appetite, satiation, vomiting and nausea in five healthy volunteers before and directly after nutrient-drink infusion ($P<0.05$). Data are expressed as percentage (%) of a VAS scale (10 mm = 100%)

	Before nutrient drink			*After nutrient drink*		
	Placebo	*Liraglutide*	P-*value*	*Placebo*	*Liraglutide*	P-*value*
Appetite	63.2 ± 13.6	45.3 ± 7.9	$P=0.19$	24.1 ± 9.6	11.3 ± 6.4	$P=0.50$
Satiation	55.5 ± 4.4	33.3 ± 8.5	$P=0.39$	65.5 ± 4.4	73.8 ± 12.5	$P=0.88$
Vomiting	4.5 ± 0.2	3.6 ± 2.7	$P=0.34$	40.1 ± 10.2	48.6 ± 10.5	$P=0.7$
Nausea	0.4 ± 0.4	2.5 ± 1.7	$P=0.41$	1.1 ± 2.9	11.1 ± 1.9	$P<0.05$

where we indeed showed that 0.6 mg liraglutide significantly decreased the postprandial balloon-volume increase. These results were unexpected, as it was previously shown that GLP-1 increased both fasting and postprandial gastric volume in humans,[11–13] using single photon emission computed tomography (SPECT).[11–13] SPECT combines imaging of the gastric wall using intravenously administered ^{99m}Tc pertechnetate. The image analysis obtained provides a measure of gastric volume, however, it is unclear whether volume changes represent changes in gastric tone. A validation study where subjects underwent SPECT and barostat on separate occasions showed poor correlation between the two techniques with respect to meal-induced accommodation.[30] In addition, meal-induced accommodation assessed by SPECT did not differ from ingested-meal volumes. It was concluded that in the absence of a distending pressure, gastric volumes determined by SPECT scanning reflect ingested volumes rather than gastric relaxation and this is likely to account for the poor correlation between the two techniques.[30] Moreover, some authors suggested that GLP-1 may increase postprandial gastric volume by slowing gastric emptying, however, it is known that GLP-1 reduces gastric secretion,[31] which would be anticipated to reduce and not increase gastric volumes. Either way, differences observed between the SPECT study and the present results might well be explained by these methodological differences.

Alternatively, differences between liraglutide and GLP-1 can be attributed to a slightly different pharmacological profile: the studies that analyze the effect of GLP-1 on gastric accommodation used physiological and supraphysiological doses;[11–13] indeed, although studies *in vitro* suggest that liraglutide binds GLP-1 receptors with similar potency as native GLP-1,[17] clinical data indicate that the spectrum and magnitude of actions of GLP-1 and liraglutide are not identical.[17] Thus it is difficult to confirm if the used doses are similar regarding the binding with GLP-1 receptors.

A second readout of this study was satiation. We observed that the acute administration of low doses of liraglutide (0.3 mg or 0.6 mg) did not significantly alter meal-induced satiation during a nutrient-meal challenge. However, the study was not powered to detect significant differences in meal-induced satiation. In addition, our results are in agreement with other studies demonstrating that chronic administration of low dose of liraglutide (0.6 mg daily) does not affect the appetite whereas higher doses (>1.2 mg) decreased appetite in HVs and diabetic patients.[21,22,32] In these studies, high dose of liraglutide was also associated with gastrointestinal adverse effects such as nausea, diarrhea and vomiting.[19–22] Also in our study, 1.2 mg liraglutide significantly decreased the maximum-tolerated volume of the nutrient test meal, most likely as this dose was associated with major nausea and vomiting.

Dyspeptic symptoms as nausea, vomiting, early satiation and decreased appetite are linked to weight loss.[32] Several clinical studies have demonstrated that chronic administration of liraglutide at doses >1.2 mg caused weight loss and this has been attributed to a delay in gastric emptying and to sensations of early fullness or satiation.[20–22,33] The effect of liraglutide on gastric motility has not been well studied, but some studies have demonstrated that low doses of liraglutide ($0.6\,mg\,d^{-1}$ and $6\,\mu g\,kg^{-1}\,d^{-1}$) had no significant effect on gastric emptying,[34,35] whereas higher doses ($1.8\,mg^{-1}\,d^{-1}$ and $10\,\mu g\,kg^{-1}\,d^{-1}$) caused a slight delay.[36] On the other hand, it has not been established that delayed gastric emptying contributes to weight loss, and abnormalities of gastric reservoir capacity (gastric accommodation) were shown to be more closely associated with weight loss.[5] Indeed, we have previously shown that impaired gastric accommodation in functional dyspeptic patients is associated with early satiation and weight loss.[2,3] In the present study, impaired gastric accommodation was not correlated to increased satiation, whereas 1.2 mg liraglutide decreased the volume consumed, but also induced nausea. This study does not confirm a possible relationship between gastric accommodation and satiation.

In conclusion, low doses of liraglutide inhibit gastric accommodation in HVs, whereas this was not associated with altered perception, discomfort thresholds to gastric distention or satiation. Administration of 0.3 or 0.6 mg of liraglutide was well tolerated, however, 1.2 mg of liraglutide induced nausea and vomiting, and decreased the maximum volume nutrients consumed.

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