Improvement in binge eating in non-diabetic obese individuals after 3 months of treatment with liraglutide — A pilot study

**KEYWORDS**

Binge eating; Obesity; Glucagon-like peptide-1; Liraglutide; Ghrelin

**Summary** We examined the effects of liraglutide, a glucagon-like peptide-1 analogue on appetite and plasma ghrelin in non-diabetic obese participants with subclinical binge eating (BE). Forty-four obese BE participants (mean age: 34 ± 9 years, BMI: 35.9 ± 4.2 kg/m²) were randomly assigned to intervention or control groups for 12 weeks. All participants received standard advice for diet and exercise. Binge eating score, ghrelin levels and other anthropometric variables were evaluated at baseline and at the end of the study. Participants who received liraglutide showed significant improvement in binge eating, accompanied by reduction in body weight, BMI, waist circumference, systolic blood pressure, fasting glucose and total cholesterol. Ghrelin levels were significantly increased which may potentially diminish the weight loss effects of liraglutide beyond the intervention.

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**Introduction**

Binge eating has gained much attention because of its importance in influencing weight gain. Effective therapy to reduce binge eating is scarce. A binge episode is characterised by out-of-control eating of large amount of food in a short time period [1]. About 7.5–30% of obese individuals seeking treatment have binge eating disorder (BED) or subclinical binge eating disorder (BE) [2].

Glucagon-like peptide-1 (GLP-1) secreted within the terminal ileum influences appetite by its dual mechanisms of inhibiting appetite centres in the brain and delaying gastric emptying [3]. We postulate that these satiating effects of GLP-1 may potentially reduce binge eating. Liraglutide is an analogue of GLP-1, with 97% similarity in structure [4].

Ghrelin is an appetite-stimulating hormone secreted within the gastric mucosa. Human studies demonstrated increased in hunger and food consumption following the administration of ghrelin in comparison to placebo [5]. In this study, we examined the efficacy of liraglutide on appetite and plasma ghrelin in non-diabetic obese participants with BE. To the best of our knowledge, there are no previous similar studies.

**Method**

This was a randomised, prospective, controlled trial conducted at a tertiary medical institution. The validated questionnaire, Binge Eating Scale (BES) was...
used to identify binge eaters [6,7]. BES has been proven to be useful to identify binge eaters and to monitor treatment effectiveness [6]. Based on BES scores, individuals scoring below 18 would be categorised as non-binge.

Forty-four obese binge eaters were randomly assigned to intervention (liraglutide 1.8 mg, diet and exercise) or control (diet and exercise) groups for 12 weeks. Participants were assessed at weeks 1, 6 and 12. BES, ghrelin levels and other anthropometric variables were obtained at baseline and at the end of the study. Participants were excluded if they had a history of taking medications that may affect weight and appetite, contraindications to liraglutide, and any chronic illnesses such as diabetes mellitus, impaired glucose tolerance, and cardiovascular diseases. The study was approved by our institutional review board and conducted in accordance with the Declaration of Helsinki using good clinical practice. Written consent was obtained from all participants.

Data were analysed using SPSS version-19. Independent T-test was used to compare between two groups and paired t-test within a group. Two-hour area under the curve (AUC) was calculated using trapezoidal method. Repeated measures ANOVA were used to analyse the changes in ghrelin concentration over time between the two groups. Two-tailed p < .05 was required for statistical significance.

### Results and discussion

Both groups were comparable at baseline. Participants who received liraglutide had significant reductions in BES [20 (IQR 18–27) to 11 (IQR 7–16), p < 0.001], body weight (94.54 ± 18.14 kg to 90.14 ± 19.70 kg, p < 0.001), BMI (36.15 ± 3.84 kg/m² to 34.40 ± 4.77 kg/m², p < 0.001), waist circumference (103.91 ± 13.65 cm to 100.20 ± 14.02 cm, p = 0.044], systolic blood pressure (130 ± 15 mmHg to 123 ± 17 mmHg, p = 0.042), fasting glucose (5.06 ± 0.52 mmol/L to 4.83 ± 0.48 mmol/L, p = 0.027) and total cholesterol (5.18 ± 0.86 mmol/L to 5.15 ± 0.46 mmol/L, p = 0.796) (see Table 1). 81% (n = 17/21) of those receiving liraglutide improved from binge eating to non-binge eating category. There have been

<table>
<thead>
<tr>
<th>Table 1</th>
<th>BES and other parameters at baseline and after 12 weeks intervention in the two study groups.</th>
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<tr>
<td></td>
<td>Liraglutide (n = 21)</td>
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<tr>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td>BES (mmol/L)</td>
<td>20 (18–27)</td>
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<tr>
<td>Body weight (kg)</td>
<td>94.54 ± 18.14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.15 ± 3.84</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>103.91 ± 13.65</td>
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<tr>
<td>Hip circumference (cm)</td>
<td>120.36 ± 8.70</td>
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<tr>
<td>Waist to hip ratio</td>
<td>0.86 ± 0.08</td>
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<td>Systolic BP (mmHg)</td>
<td>130 ± 15</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td>76 ± 11</td>
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<tr>
<td>Fasting glucose (mmol/L)</td>
<td>5.06 ± 0.52</td>
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<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.18 ± 0.86</td>
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<tr>
<td>TG (mmol/L)</td>
<td>1.37 ± 0.51</td>
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<tr>
<td>LDL (mmol/L)</td>
<td>3.34 ± 0.83</td>
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<tr>
<td>HDL (mmol/L)</td>
<td>1.25 ± 0.27</td>
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* p value of ≤0.05 is considered statistically significant.
Improvement in binge eating with liraglutide

Figure 1  Ghrelin levels pre- and postprandial at baseline and after intervention period in the treatment (a) and control (b) groups. A 460 kcal standard meal was given at time 0 min. Mean ± SE, n = 21 subjects per group. *p < 0.05.

no studies to date on the effect of pharmacology treatment of BE in non-diabetic obese individuals. In studies on patients with BED, about 50% of patients stopped binge eating after cognitive behavioural therapy (CBT) [8] and 47–74% recovered with CBT plus fluoxetine [9]. Approximately 58% of patients attained remission after treatment with topiramate [10]. However, weight loss was minimal with those treatments. In this study, 50% of participants who received liraglutide obtained 5% weight loss which is associated with reductions in cardiovascular risks. We demonstrated here the effect of GLP-1 which was independent of glucose levels and is efficacious in non-diabetic obese individuals. In our study, 2 patients developed nausea with liraglutide, however this did not lead to withdrawal. Nausea resolved with continued treatment.

One important aspect of this study is the use of ghrelin as a biochemical measure of hunger. There was a significant increase in ghrelin at certain time intervals after liraglutide therapy, at 15 min (6.90 ± 2.75 ng/ml to 8.50 ± 2.57, p = 0.017); at 60 min (7.24 ± 2.78 to 8.40 ± 3.38, p = 0.037); at 90 min (6.71 ± 3.07 to 8.08 ± 3.03, p = 0.040) and at 120 min (6.64 ± 2.83 to 8.32 ± 2.35, p = 0.005) (Fig. 1). AUC ghrelin also increased in the liraglutide group (855.55 ± 293.61 ng/ml min to 1002.77 ± 322.96 ng/ml min, p = 0.018) but not within the control group. The increase in ghrelin
observed in our study is similar to the rise of ghrelin levels with diet-induced weight loss, suggesting an adaptation response to constrain weight loss [11].

The limitations of our exploratory pilot study are that it is not a double-blinded study and we did not include a placebo injection. Furthermore, BE was only measured with questionnaire instead of an additional clinical interview. However, our study provides a rationale for future studies.

In summary, twelve weeks’ therapy with liraglutide, in non-diabetic obese individuals, significantly improved BE, accompanied by reduction in body weight, and other cardiovascular risk factors. Ghrelin levels significantly increased which have the potential to diminish the weight loss effects of liraglutide beyond the intervention.

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Conflict of interest
The authors have nothing to disclose.

References

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