Treatment With a Ghrelin Agonist in Outpatient Women With Anorexia Nervosa: A Randomized Clinical Trial

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ABSTRACT

Objective: To assess the effects of relamorelin—an agonist of the appetite-stimulating hormone ghrelin, which has effects on gastric emptying—on (1) weight gain and (2) gastric emptying in women with anorexia nervosa.

Methods: In a randomized, double-blind, placebo-controlled design, the effects of the ghrelin agonist relamorelin were studied in 22 outpatient women with anorexia nervosa, diagnosed using *DSM-5* criteria. The study was conducted at the Massachusetts General Hospital Clinical Research Center between March 11, 2013, and February 26, 2015. Ten participants were randomly assigned to relamorelin 100 µg subcutaneously daily (mean ± SEM age: 28.9 ± 2.4 y), and 12 were randomly assigned to placebo (28.9 ± 1.9 y). We measured changes in weight and gastric emptying time using a gastric emptying breath test (GEBT) for relamorelin versus placebo after 4 weeks of treatment.

Results: At baseline, subjects did not differ in weight, plasma ghrelin levels, or gastric emptying time. Three subjects randomized to relamorelin stopped use of the study medication due to reported feelings of increased hunger. After 4 weeks, there was a trend toward an increase in weight in participants randomized to relamorelin (mean ± SEM change: 0.86 ± 0.40 kg) compared to placebo (0.04 ± 0.28 kg; $P = .07$), and gastric emptying time was significantly shorter in patients taking relamorelin (median [interquartile range]: 58.0 [51.0, 78.0] minutes) compared to placebo (85.0 [75.8,100.5] minutes; $P = .03$).

Conclusions: Treatment with a ghrelin agonist in women with anorexia nervosa significantly decreases gastric emptying time, leads to a trend in weight gain after only 4 weeks, and is well-tolerated. Further study is necessary to determine the long-term safety and efficacy of a ghrelin agonist in the treatment of anorexia nervosa.

Trial Registration: ClinicalTrials.gov identifier: NCT01642550

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Anorexia nervosa, a psychiatric disorder with a lifetime prevalence of up to 2.2% in women,[1] is characterized by an extreme fear of weight gain and inappropriately low caloric intake. Nutritional rehabilitation and psychotherapy are first-line treatments for anorexia nervosa, but relapse rates remain near 40%–50% even many years after the initial diagnosis.[2,3] Pharmacologic agents, including selective serotonin reuptake inhibitors and atypical antipsychotics, have been studied, but definitive benefit has not been demonstrated, and there are no approved therapies for anorexia nervosa.[4] As anorexia nervosa has among the highest mortality rates of any psychiatric illness,[5] the need for effective treatments is critical. Importantly, rates of delayed gastric emptying are reported to be as high as 50%–80% in this population,[6–8] and associated gastrointestinal symptoms may interfere with eating and impede nutritional recovery.

Ghrelin is an orexigenic hormone produced by the fundal cells of the stomach. Its active form, acylated ghrelin, binds to growth hormone secretagogue receptor 1a (GHS-R1a). In addition to stimulating appetite, ghrelin is a potent stimulator of gastric motility. Despite the fact that total ghrelin levels are elevated in girls and women with anorexia nervosa,[9–11] women with anorexia nervosa report less hunger than healthy controls.[12] This discrepancy may be due to ghrelin resistance in individuals with anorexia nervosa[13] or to differences in the ratio of the active versus degraded forms of ghrelin in women with anorexia nervosa compared with healthy controls.[14] Relamorelin (Motus Therapeutics, formerly Rhythm Pharmaceuticals, Boston, Massachusetts) is a potent agonist of GHS-R1a. In diabetic individuals with gastroparesis, relamorelin has been shown to accelerate gastric emptying.[15] Although prior studies have demonstrated improvements in gastric emptying in anorexia nervosa with prokinetic agents, including erythromycin [16] and metoclopramide,[17] these agents are not approved for treatment of anorexia nervosa, and side effects may preclude long-term use. Therefore, we hypothesized that in women with anorexia nervosa, treatment with a ghrelin agonist—a prokinetic agent with the additional potential to stimulate appetite—would result in (1) weight gain and (2) improved gastric emptying. We investigated this hypothesis in a 4-week double-blind, randomized, placebo-controlled clinical study.

Clinical Points

- Anorexia nervosa has a high relapse rate, and there are no approved medical therapies for this disorder.
- Ghrelin is an appetite-stimulating hormone with effects on gastric emptying. Treatment with a ghrelin agonist may lead to improved gastric emptying and weight gain in women with anorexia nervosa.

METHODS

Study Participants

Study participants were recruited through referrals from local eating disorder providers and on-line advertisements and were enrolled in the study between March 11, 2013, and February 26, 2015. Participants had to meet *DSM-5* criteria[18] for anorexia nervosa and have self-reported gastrointestinal symptoms (such as fullness, bloating, and constipation). All subjects were outpatients at the time of enrollment and none were receiving hyperalimentation therapy or tube feedings. Inclusion criteria also required subjects to be on a stable medication regimen for at least 2 weeks prior to their baseline visit. Exclusion criteria included pregnancy, diabetes mellitus, peptic ulcer disease, inflammatory bowel disease, celiac disease, history of gastrointestinal surgery, history of a malignancy, abnormal thyroid function, active substance abuse, evidence of severe depression as measured by a Beck Depression Inventory-2 (BDI-2)[19] score of ≥ 29, and use of agents that might affect gastric motility (including metoclopramide, erythromycin, 5-HT_3 antiemetics, or opiates) within the 2 weeks prior to the baseline visit.

Study Protocol

Subjects who met inclusion criteria after a screening visit presented for a baseline visit at the Massachusetts General Hospital Clinical Research Center (MGH CRC). At the baseline visit, subjects were instructed on how to self-administer the study medication (relamorelin or masked placebo), and after the completion of the baseline visit procedures, they self-administered the first dose. Subjects self-administered the study medication (relamorelin 100 µg subcutaneously or placebo) every morning daily for 4 weeks and returned to the MGH CRC once weekly for a total of 5 weeks. At all of the weekly visits, subjects had a physical examination, were weighed on an electronic scale while wearing a hospital gown, and completed a visual analog scale (VAS) appetite assessment[20] after an overnight fast. At the baseline visit, subjects' height was measured as the mean of 3 readings on a single stadiometer, and elbow breadth (for estimation of frame size) was measured using calipers and compared to norms based on NHANES-I data. Body mass index was calculated using the formula weight (kg)/height (meter)^2, and percentage of ideal body weight was calculated based on 1983 Metropolitan Life Height and Weight tables.[21] At the baseline and week 4 visits, laboratory values were obtained after an overnight fast, resting energy expenditure was measured using indirect calorimetry (Vmax Encore 29 metabolic cart; Carefusion, San Diego, California), and a gastric emptying breath test (GEBT; Advanced Breath Diagnostics, Brentwood, Tennessee) was performed with a meal containing ^{13}C-spirulina platensis. Subjects also completed the BDI-2[19] and the Patient Assessment of Upper Gastrointestinal Symptom Severity Index (PAGI-SYM)[22] at baseline, week 2, and week 4.

The study was approved by the Partners Institutional Review Board and complied with the Health Insurance Portability and Accountability Act guidelines. Written informed consent was obtained from all subjects. The study was registered at clinicaltrials.gov (identifier: NCT01642550) on July 13, 2012.

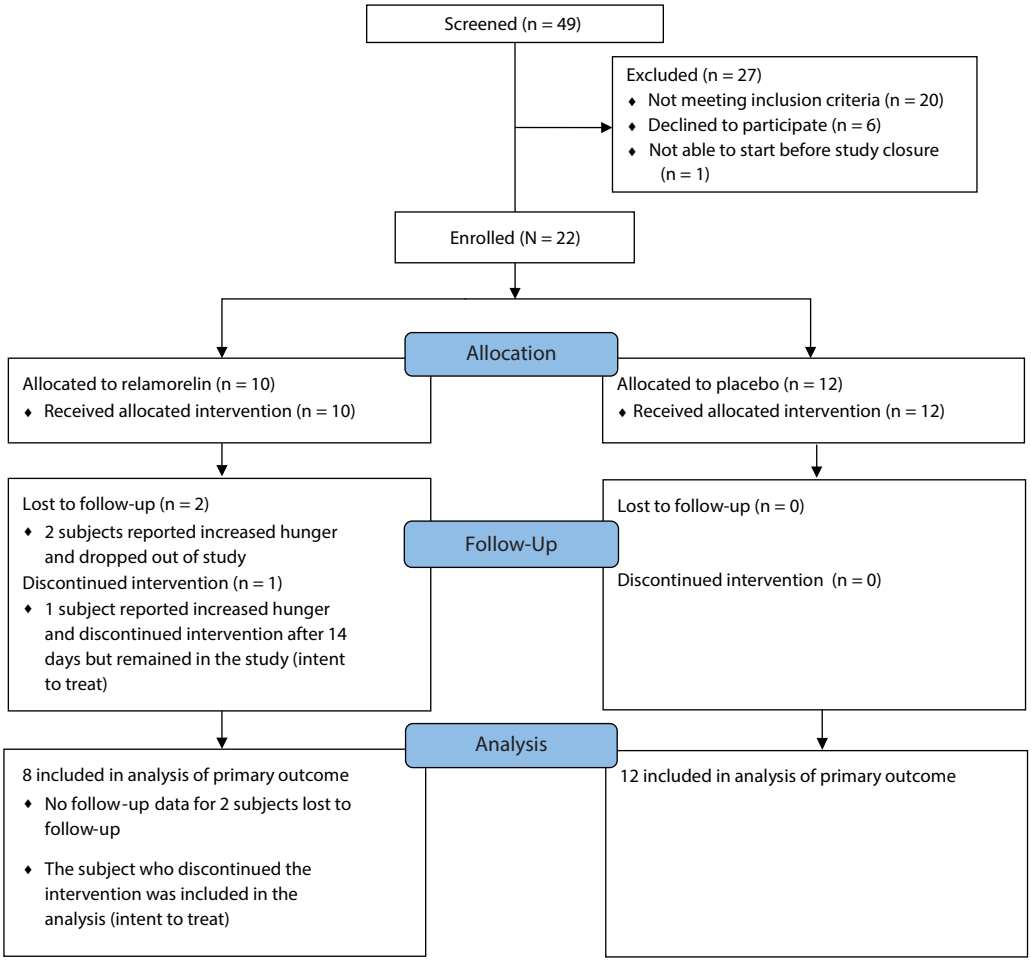
Biochemical Assessment

Total plasma ghrelin levels were measured by ELISA (EMD Millipore, Billerica, Massachusetts) with an intraassay coefficient of variation (CV) of 1.32% and an interassay CV of 6.62%. Plasma was collected in tubes containing phenylmethylsulfonyl fluoride/hydrochloric acid to measure acylated ghrelin by ELISA (EMD Millipore, Billerica, Massachusetts) with an intraassay CV of 3.09% and an interassay CV of 7.56% and desacyl ghrelin by ELISA (Cayman Chemical, Ann Arbor, Michigan) with an intraassay CV of 6.93% and an interassay CV of 7.23%. Insulin-like growth factor 1 (IGF-1) was measured by a luminescent immunoassay analyzer (ISYS Analyzer; Immunodiagnostics, Woburn, Massachusetts). IGF-1 was measured after acid extraction to minimize interference with binding proteins. The intraassay CV for IGF-1 was 2.2%, and the interassay CV was 5.1%.

Statistical Analysis

A sample size of 20 participants was planned using a standard deviation for a 4-week change in weight of 1 kg. Statistical analysis was performed using JMP Pro 11.0 (SAS Institute, Cary, North Carolina) software. Means and standard error of the mean (SEM) measurements are reported and compared using the Student *t* test unless the data were non-normally distributed, in which case the Wilcoxon rank sum test was used. Percentages were compared using the Fisher exact test. One acylated ghrelin level at baseline and 3 acylated ghrelin values (2 from the relamorelin group and 1 from the placebo group) at the week 4 time-point were below the detection limit of the assay. Since the mean and median acylated ghrelin levels at week 4 for the relamorelin group were lower than those of the placebo group, these samples were left out of the analysis (for acylated ghrelin only), rather than substituting a value less than the detection limit, to minimize bias. A longitudinal general linear mixed-effects model was used to detect a between-group difference of the longitudinal mean changes by testing the group × time interaction for endpoints in which more than 2 time-points were measured. Multivariable analyses were performed using least-squares linear regression to control for confounders.

Figure 1. CONSORT Diagram



A P value of $< .05$ on a 2-tailed test was used to indicate statistical significance, and data were analyzed using an intent-to-treat analysis.

RESULTS

Study Participants

Forty-nine individuals were screened for the study, and a total of 29 were found to be eligible (Figure 1). Reasons for ineligibility included not meeting *DSM-5* criteria for anorexia nervosa (n = 9), abnormal screening laboratory values (n = 3), BDI-2 score of ≥ 29 (n = 5), history of a malignancy (n = 1), history of intestinal surgery (n = 1), and participation in another clinical trial within the last 30 days (n = 1). Twenty-two subjects enrolled in the study, and 7 eligible subjects chose not to enroll. Reasons for not participating included the inability to commit the time required for the study (n = 2), loss of interest in participating (n = 4), and inability to start the study before study closure (n = 1).

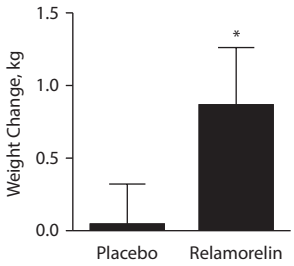
Baseline characteristics of the study participants are listed in Table 1. Study subjects in both groups were of similar percentage of ideal body weight (relamorelin: 79.9% ± 1.5% vs placebo: 81.0% ± 2.1%; $P = .67$) and had similar median (interquartile range [IQR]) baseline gastric emptying times: relamorelin: 89.0 (69.5, 110.8) minutes versus placebo: 85.5 (74.0, 125.8) minutes; $P = .60$). Participants in the relamorelin group had a higher baseline score for the VAS hunger assessment (relamorelin: 6.3 [2.2, 8.1] cm vs placebo: 3.0 [1.0, 5.5] cm), but this difference was not statistically significant ($P = .15$). Nine subjects (75%) randomized to placebo and all 10 subjects (100%) randomized to relamorelin ($P = .22$) were receiving long-term outpatient therapy, which continued during the course of the study. None of the subjects was transitioned to inpatient therapy or a higher level of care during the course of the study. None of the subjects had any changes to treatment during the study except that 1 subject randomized to relamorelin and 1 subject randomized to placebo each had a dose increase in medications (escitalopram and duloxetine, respectively) during the course of the study. There was a mean ± SEM of 31.3 ± 4.5 days between the screening visit and the baseline visit for subjects in the study. During this month prior to the initiation of study drug (which occurred at the baseline visit), the mean change in weight was similar in both groups (relamorelin: −0.20 ± 0.35 kg and placebo: −0.25 ± 0.44 kg; $P = .93$).

Table 1. Baseline Clinical Characteristics of Study Participants[a]

Variable	Relamorelin (n = 10)	Placebo (n = 12)	*P* Value
Age, y	28.9 ± 2.4	28.9 ± 1.9	.99
Percentage of ideal body weight	79.9 ± 1.5	81.0 ± 2.1	.67
Weight, kg	48.1 ± 1.5	48.9 ± 1.8	.73
Height, cm	165.2 ± 2.3	165.3 ± 1.9	.97
BMI, kg/m^2	17.6 ± 0.4	17.8 ± 0.4	.58
Duration of anorexia nervosa, y	13.2 ± 2.2	14.8 ± 2.2	.60
Gastric emptying time, median (IQR), min	89.0 (69.5, 110.8)	85.5 (74.0, 125.8)	.60
Resting energy expenditure, kcal/d	1,040 ± 40	1,055 ± 53	.83
Beck Depression Inventory-2 score	15.2 ± 2.8	12.3 ± 2.1	.41
Visual analog scale—hungry score, median (IQR), cm	6.3 (2.2, 8.1)	3.0 (1.0, 5.5)	.15
Total ghrelin,[b] median (IQR), pg/mL	878 (722, 1,191)	1131 (825, 1,263)	.34
Acylated ghrelin,[b] median (IQR), pg/mL	162 (118, 293)	140 (52, 366)	.65
Desacyl ghrelin,[b] median (IQR), pg/mL	422 (225, 678)	444 (318, 599)	.87
IGF-1, ng/mL	156 ± 10	171 ± 14	.39
Serum glucose, mg/dL	77.8 ± 2.3	83.1 ± 2.4	.13

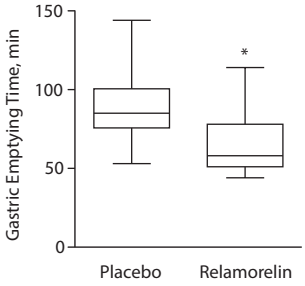
[a]Values shown as mean ± SEM unless otherwise noted.
[b]Values are plasma levels.
Abbreviations: BMI = body mass index, IGF-1 = insulin-like growth factor 1, IQR = interquartile range.

Figure 2. Mean Weight Gain in Women With Anorexia Nervosa Randomized to Relamorelin Versus Placebo After 4 Weeks of Treatment[a]



[a]Values are shown as mean ± SEM.
*The mean weight gain was greater with relamorelin than with placebo ($P < .07$).

Figure 3. Median Gastric Emptying Time in Women Randomized to Relamorelin Versus Placebo After 4 Weeks of Treatment[a]



[a]Boxes represent medians and interquartile ranges, and whisker plots represent maximum and minimum values.
*The median gastric emptying time was significantly shorter with relamorelin than with placebo ($P = .03$).

Change in Weight

Participants randomized to relamorelin gained more weight (0.86 ± 0.40 kg; range, −0.3 to 2.8 kg) as compared to participants in the placebo group (0.04 ± 0.28 kg; range, −1.6 to 2.1 kg), although there was only a trend toward statistical significance ($P < .07$) (Figure 2). The results were similar ($P = .06$) when controlling for baseline VAS hunger score. Of the 20 subjects for whom we have follow-up data, 7 (87.5%) of the 8 subjects randomized to relamorelin gained weight between baseline and week 4 whereas only 6 (50%) of the 12 subjects randomized to placebo gained weight.

Change in Gastric Emptying Time

After 4 weeks of treatment, participants randomized to relamorelin had a significantly shorter median (IQR) gastric emptying time as compared to those randomized to placebo (relamorelin: 58.0 [51.0, 78.0] minutes vs placebo: 85.0 [75.8, 100.5] minutes; $P = .03$) (Figure 3). The mean ± SEM percent decrease in gastric emptying time was also significantly greater in the relamorelin group (−24.3% ± 3.9%) as compared to placebo (−5.1% ± 7.3%; $P = .03$).

Change in VAS Hunger Score, Self-Reported Gastrointestinal Symptoms, and Resting Energy Expenditure

Change in mean ± SEM VAS hunger score was similar in both groups after 4 weeks of treatment (relamorelin: −0.48 ± 0.77 cm vs placebo: 0.63 ± 0.51 cm; $P = .26$), as was median (IQR) change in self-reported gastrointestinal symptoms (relamorelin: −0.52 [−0.91, 0.06] vs placebo: −0.23 [−0.71, 0.06]; $P = .65$). On repeated-measures analysis, there was no significant group × time interaction with respect to VAS hunger score ($P = .35$) or gastrointestinal symptoms ($P = .61$). Mean ± SEM resting energy expenditure, as measured by indirect calorimetry, was similar in both groups at week 4 (relamorelin: 1,098 ± 39 kcal/d vs placebo: 1,063 ± 49 kcal/d; $P = .59$), as was median (IQR) percent change in resting energy expenditure after 4 weeks of

Table 2. Adverse Effects Experienced by Study Participants

Adverse Effect	Relamorelin (n = 8)[a]	Placebo (n = 12)[a]	*P* Value
Injection site ecchymoses, bruising, erythema	4 (50)	4 (33.3)	.65
Electrolyte abnormalities	2 (25)	4 (33.3)	.99
Dizziness			
All participants	5 (62.5)	1 (8.3)	.02
Participants not reporting symptom at baseline	3/6 (50)	0/11 (0)	.03
Fatigue			
All participants	7 (87.5)	5 (41.7)	.07
Participants not reporting symptom at baseline	2/3 (66.7)	2/8 (25)	.49
Abdominal pain/cramping			
All participants	7 (87.5)	9 (75)	.62
Participants not reporting symptom at baseline	1/2 (50)	3/5 (60)	.99
Muscle weakness			
All participants	1 (12.5)	2 (16.7)	.99
Participants not reporting symptom at baseline	1/8 (12.5)	1/11 (9.1)	.99
Hyperhidrosis			
All participants	2 (25)	1 (8.3)	.54
Participants not reporting symptom at baseline	1/7 (14.3)	0/10 (0)	.41

[a]Values shown as n (%) or n/total n (%).

treatment (relamorelin: 0.3% [−4.7%, 11.7%] vs placebo: −0.8% [−8.2%, 7.4%]; $P = .46$).

Change in Hormone Levels

Total, desacyl, and acylated ghrelin. After 4 weeks of treatment, median (IQR) plasma acylated ghrelin levels decreased in the relamorelin group (−47.3% [−91.7%, 5.8%]) as compared to placebo (114.7% [−36.8%, 329.3%]), and this difference was statistically significant ($P = .04$). In contrast, the mean ± SEM percent change in plasma total ghrelin (relamorelin: −7.5% ± 8.0% vs placebo: 4.4% ± 5.7%) and desacyl ghrelin (relamorelin: −5.5% ± 13.5% vs placebo: 2.1% ± 9.5%) was similar in both groups ($P = .25$ and $P = .65$, respectively).

Growth hormone axis. IGF-1 levels increased significantly in the relamorelin group as compared to placebo after 4 weeks of treatment. IGF-1 levels increased by a mean ± SEM of 28.8 ± 9.9 ng/mL in the relamorelin group as compared to decreasing by 11.3 ± 5.8 ng/mL in the placebo group ($P < .01$). This corresponds to a mean ± SEM percent change in IGF-1 levels of 18.0% ± 6.1% after 4 weeks of relamorelin as compared to −5.8% ± 2.9% after 4 weeks of placebo ($P < .01$). These differences remained significant after controlling for change in weight ($P < .01$ for both).

Adverse Events and Tolerability

The study drug was well tolerated during this 4-week study. Mean ± SEM depression severity scores (BDI-2) decreased similarly in both groups after 4 weeks of treatment (relamorelin: −1.5 ± 1.3 vs placebo: −1.1 ± 1.5; $P = .84$). Two participants, both randomized to relamorelin, dropped out of the study. One dropped out after 4 days of using relamorelin, and the second dropped out after 12 days. Both reported that they were discontinuing the study medication due to a significant increase in hunger. A third participant, also randomized to relamorelin, remained in the study but stopped using the study drug after 14 days due to experiencing hunger and weight gain (weight increased 1.6 kg during the 14 days on which she was on the study medication). The remaining 19 study subjects completed the study.

Adverse events are reported in Table 2. Four subjects in each group experienced minor injection site reactions (bruising, ecchymoses, and/or erythema), and all reactions resolved spontaneously. One participant, randomized to relamorelin, developed abdominal cramping and became diaphoretic 20 minutes after her initial dose of relamorelin but did not have a recurrence of these symptoms on continuing treatment and successfully completed the study. Two subjects who completed the study and were randomized to relamorelin had triglyceride levels > 150 mg/dL during the study (1 peaked at 199 mg/dL and the other at 153 mg/dL), but by the week 4 visit, both subjects had triglyceride levels < 100 mg/dL. On repeated-measures analysis, there was no significant group × time interaction with respect to triglyceride levels ($P = .25$).

Of the 17 subjects who did not report dizziness at baseline, no subjects in the placebo group (0 of 11) and 3 (50%) of 6 in the relamorelin group reported experiencing dizziness during the study ($P = .03$).

DISCUSSION

We have shown that in women with anorexia nervosa, treatment with a ghrelin agonist significantly decreases gastric emptying time. Although we did not find significant

differences in VAS hunger score in the relamorelin group as compared to the placebo group after 4 weeks of treatment, 3 participants stopped use of relamorelin due to symptoms of increased hunger and 2 dropped out of the study for that reason. We also found that the relamorelin group gained more weight than the placebo group, although there was only a trend toward significance for this outcome.

Desacyl ghrelin constitutes the majority of circulating levels of ghrelin and does not bind to GHS-R1a. Desacyl ghrelin was thought to be an inactive form of ghrelin, although recently it has been shown to have potential antighrelin effects including blocking ghrelin's appetite-stimulatory effects.[23] Desacyl ghrelin levels are higher in women with anorexia nervosa as compared to healthy controls,[14] which may explain why women with anorexia nervosa report lower levels of hunger when compared to normal-weight controls[12] despite the fact that women with anorexia nervosa have higher total ghrelin levels. In anorexia nervosa, levels of acylated ghrelin—the orexigenic form of ghrelin—have been reported in a number of studies[14,24] to be lower than or similar to those of normal-weight controls, and therefore treatment with acylated ghrelin or a GHS-R1a agonist may be useful for stimulating hunger in anorexia nervosa.

Gastrointestinal symptoms are common in individuals with anorexia nervosa.[25] Frequently reported symptoms, including postprandial fullness and abdominal distention,[26] may impede recovery by making it difficult for individuals with anorexia nervosa to consume an adequate number of calories. Some of the gastrointestinal symptoms reported in anorexia nervosa may be due to delayed gastric emptying, which is reported in as many as 50%–80% of individuals with anorexia nervosa.[6–8] Therefore, treatment with an agent that improves gastric emptying, such as a ghrelin agonist, could potentially aid in the nutritional rehabilitation of individuals with anorexia nervosa. In fact, prior studies involving prokinetic agents[16,17] have demonstrated improvements in gastric emptying and weight gain in anorexia nervosa, yet these agents are not approved for use in the treatment of anorexia nervosa, very likely because of the side effects associated with long-term use of medications such as metoclopramide.

Ghrelin has been used as a potential appetite stimulant in a number of patient populations,[27] including women with anorexia nervosa. A prior study investigating the effects of a human ghrelin infusion in 5 individuals with anorexia nervosa[28] demonstrated an increase in food intake during and after the infusion period as compared to the pretreatment period. But because there was no control group—all 5 participants received ghrelin—and because all of the participants were hospitalized for hyperalimentation therapy, the benefit of ghrelin independent of hyperalimentation therapy is difficult to discern.[28] Because most individuals with anorexia nervosa are treated as outpatients and not hospitalized, the results of our study are generalizable to a slightly broader population of individuals with anorexia nervosa, as all of our participants were outpatients and none received hyperalimentation therapy during the course of the study. Yet, importantly, all 3 subjects who discontinued study drug during the course of the study were randomized to relamorelin, which suggests that this treatment may not be tolerated by all individuals with anorexia nervosa. Therefore, further study will be necessary to carefully determine which patients may best benefit from this potential treatment.

Acylated ghrelin, the form that is able to bind to GHS-R1a, not only stimulates appetite and gastric motility but also is a potent activator of the growth hormone–IGF-1 axis. In this 4-week study, we also found a significant increase in IGF-1 in the relamorelin group as compared to the placebo group, even after controlling for change in weight. Given that GHS-R1a is a stimulator of growth hormone secretion, it would not be surprising but for the fact that women with anorexia nervosa are growth hormone resistant—their GH levels are normal or elevated in the setting of low IGF-1 levels.[29–31] This resistance state allows for growth hormone to stimulate lipolysis and fat mobilization[32] to provide critical nutrients for survival in this state of chronic undernutrition, while the low IGF-1 levels allow for minimization of energy expenditure on growth. We have previously shown that treatment with supraphysiologic doses of recombinant human growth hormone does not increase IGF-1 levels in anorexia nervosa[33] and therefore the mechanism of this rise in IGF-1 levels is unclear and warrants further study. But, importantly, IGF-1 levels have been positively associated with bone mineral density in anorexia nervosa,[34] and treatment with recombinant human IGF-1 in combination with estrogen leads to gains in bone mineral density[35] in women with anorexia nervosa, suggesting that a GHS-R1a agonist may have additional potential benefits in women with anorexia nervosa beyond weight gain alone.

Limitations of our study include its small sample size and short follow-up period. As this was a pilot study and the first use of a ghrelin agonist in women with anorexia nervosa, we designed a short-term study to minimize the potential changes in weight that may be observed if a participant is hospitalized or enters into a treatment facility. The short-term nature of the study allowed us to observe changes that are most likely attributable to the study drug rather than to changes in the treatment status of our participants, although it limits our ability to project the long-term benefits of this therapy.

In conclusion, we have shown that treatment with a ghrelin agonist significantly improves gastric motility and may be a stimulator of weight gain in women with anorexia nervosa. As there are no currently approved medical therapies for the treatment of this chronic disease characterized by significant morbidity and mortality, further study is necessary to determine the long-term efficacy and safety of a ghrelin agonist as a potential therapeutic option for individuals with anorexia nervosa.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene P. Freeman, MD, at mfreeman@psychiatrist.com.