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Intragastric Balloon-Induced Satiety is Not Mediated by Modification in Fasting or Postprandial Plasma Ghrelin Levels in Morbid Obesity

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Background: The BioEnterics Intragastric Balloon (BIB) has been proposed as an adjuvant therapy for the short-term treatment of obesity. The temporal pattern of BIB-induced satiety and whether this effect is mediated by modification of ghrelin levels is unknown.

Methods: Patients with treatment-resistant morbid obesity were invited to participate in a randomized, double-blind, sham-controlled trial of 4-month duration. Anthropometric and biochemical parameters, estimation of energy intake, and pre- and postprandial evaluation of satiety were required monthly. Ghrelin response after a standard mixed meal was scheduled prior to and 4 weeks after the endoscopic procedure.

Results: 21 out of 22 enrolled patients completed the study (17 women, 5 men; 35.9±9.9 years; BMI 50.4±7.8 kg/m^2). Pre-intervention weight decreased from 143.8±31.2 kg to 131.1±32.6 kg in Group Balloon (P<0.001) and from 138.8±24.5 kg to 129.9±25.6 kg in Group Sham (P<0.01) at the end of the study. Weight loss was not significantly different in Group Balloon and Group Sham at any time-point of the follow-up. Only patients from Group Balloon showed a temporary increased pre- and postprandial satiety, which was maximal at 4 weeks after the intervention. Total area under the curve, fasting and postprandial plasma ghrelin were not significantly different between groups at inclusion or 4 weeks after follow-up. No correlation was found between any of the satiety scores at any time-point with their comparable ghrelin levels.

Conclusion: BIB induces a temporary sense of satiety in morbidly obese patients which is not mediated by modification of fasting or postprandial levels of plasma ghrelin.

Key words: Morbid obesity, intragastric balloon, satiety, ghrelin, bariatric surgery

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Introduction

Obesity is an increasing major health problem in most industrialized countries, with substantial morbidity, mortality, and economic impact. Long-term results achieved by dietary programs, exercise, behavior therapy, and pharmacological treatments are often disappointing.[1] Bariatric surgery is the most effective treatment to sustain major weight loss in morbid obesity, but its morbidity and mortality are acceptable only after failure of conservative treatments.[2]

Promising results and a low complication rate have been reported in prospective studies with the recently introduced BioEnterics® Intragastric Balloon (BIB) system (BIB®, Allergan Inamed).[3-7] Preoperative treatment of morbidly obese patients with the temporary placement of a BIB in association with dietary restriction has been proposed, to reduce the risk of complications of surgical procedures.[8-10] The sense of fullness and delayed gastric

emptying have often been described as main effects of the intragastric balloon, but whether the BIB effect is hormonally mediated is still unknown.

Ghrelin is a 28-amino acid peptide mainly produced in the stomach and has been implicated in short- and long-term regulation of energy balance.[11-13] Plasma ghrelin levels increase preprandially and decrease after meal ingestion, suggesting a role of this hormone as a meal initiator.[13,14] In obese individuals, fasting ghrelin levels are lower than in normal-weight volunteers.[15] However, postprandial plasma ghrelin suppression is attenuated in obese patients,[16,17] a fact which may influence satiety and reinforce obesity.

In this study, we assessed the temporal pattern of BIB-induced satiety in morbidly obese patients and whether this effect is mediated by modification of pre- or postprandial levels of plasma ghrelin. We also analyzed the efficacy of short-term placement of the BIB on weight reduction in morbidly obese patients in whom failure of previous conservative treatments has been documented, by using a prospective, randomized double-blind, sham-controlled study.

Materials and Methods

Patients

Patients were consecutively selected from candidates for bariatric surgery, in accordance with the National Institutes of Health criteria and national guidelines for obesity surgery.[18,19] All patients had shown failure to sustain weight loss within a supervised weight-control program before selection as candidates for bariatric surgery. In all cases, preoperative selection was made by a team composed of an endocrinologist, bariatric surgeon and psychiatrist from University Hospital Virgen del Rocio. Only patients with no medical or psychological contraindication who agreed to comply with the follow-up controls were eligible for randomization. Other specific exclusion criteria were structural abnormalities of the GI tract, high risk for bleeding, persistent *Helicobacter pylori* (HP) infection and/or pharmacological therapy potentially interfering with the BIB effect[20] (Table 1). Persistent HP infection was defined as positive urea breath test (Tau Kit®, Isomed) in spite of proton-pump-inhibitor-based triple therapy.[21]

Table 1. BioEnterics intragastric balloon exclusion criteria

- Severe GI or hepatic disease, previous GI surgery, structural abnormalities of GI tract (hiatal hernial >5 cm) and/or lesions with increased risk of bleeding (varices, peptic ulcer or >3 gastric erosions assessed by endoscopic evaluation).
- Persistent HP infection defined as positive urea breath test (Tau Kit®, Isomed) in spite of proton-pump-inhibitor-based triple therapy (treatment twice daily for 7 days with 20 mg of omeprazole, given either with 1 g of amoxicillin and 500 mg of clarithromycin).
- Chronic therapy with steroids, NSAIDs or anticoagulants.
- Therapy with sibutramine, orlistat, selective serotonin reuptake inhibitors, antidepressants, neuroleptics and/or antihistaminic drugs.

Study Protocol

Once inclusion and exclusion criteria were assessed, patients were evaluated in the outpatient clinic, and data related to co-morbidities, anthropometric variables, biochemical measurements, satiety evaluation and energy intake were collected. Patients were randomly allocated to Group A (Balloon, 4-month follow-up after BIB placement) or Group B (Sham, 4-month follow-up after sham procedure) according to a computer program-based randomization (EpiDat). Patients in Group B were comparable to those in Group A in terms of clinical characteristics, evaluation and follow-up.

The endoscopic procedure was performed with the patient in lateral decubitus position under conscious sedation by using diazepam (2.5-5 mg I.V.) and meperidine (25-50 mg I.V.). The endoscopic procedure was similar in Groups A and B. Esophagus, stomach and duodenum were examined before balloon insertion, to exclude any structural abnormalities which would preclude insertion of the balloon. Once the instrument was retrieved, the balloon was inserted into the gastric fundus in only Group A. The inflation was performed under direct vision by using saline (600 ml) and methylene blue (10 ml). In Group A, the BIB was deflated and removed by endoscopic procedures at the end of the follow-up period.

Patients were evaluated in the outpatient clinic every day on the first post-endoscopy 3 days. After assessing oral tolerance, patients were instructed to begin a qualitative low-fat hypocaloric diet (about 55% from carbohydrates, 15% from proteins, 30% from lipids, with <10% from saturated fat). Antiemetics were prescribed

in all patients after the endoscopic procedure (ondansetron 8 mg/day) and maintained as required. All patients were put on a proton pump inhibitor (omeprazole 20 mg/day). Weight, body mass index (BMI) and excess weight loss (EWL) were recorded by a nurse every 2 weeks in the outpatient clinic, with the patient in light clothes. Body composition was recorded at the beginning of the study and monthly by means of impedanciometry (OMRON BF 300, OMRON Healthcare Europe). Patients were followed monthly by an endocrinologist, blinded to patient randomization, to assess dietary patterns, metabolic control of co-morbidities and post-endoscopy symptoms. Evaluation and follow-up were identical in Group A and B.

Data regarding biochemical measurements, satiety evaluation and energy intake were collected monthly. Ghrelin response after a standard mixed meal, as described below, was scheduled prior to and 4 weeks after the endoscopic procedure.

This study was approved by the local ethics committee. Informed consent was signed by all enrolled patients.

Biochemical and Hormonal Parameters

Blood samples were collected from an antecubital vein in prechilled tubes and immediately centrifuged. Plasma was stored at -80˚C until assayed. Human plasma leptin was determined by enzymoimmunoanalysis (Biosource Leptin Easia, Biosource Europe S.A.) in the fasting condition. The intra- and inter-assay coefficients were 3.6% and 4.9%, respectively.

Ghrelin response was determined after a standard mixed meal containing 452 Kcal (57.2 g of carbohydrates, 21.2 g of lipids, 8.0 g of proteins) consumed at 9 h AM. For preprandial ghrelin assessment, blood samples were collected 60 minutes before meal ingestion. Additional blood samples for ghrelin assessment were collected immediately before meal ingestion and at 60, 120 and 240 minutes after meal ingestion. Human plasma ghrelin was measured in duplicate by a commercial radioimmunoassay (Ghrelin RIA, Linco Research). The inter- and intra-assay coefficients were 10.0% and 14.7%, respectively.

Evaluation of Satiety

Patients were asked to complete a satiety questionnaire using a validated 100 mm Visual Analog Scale (VAS) (Figure 1) before and immediately after a standard breakfast, as described above. Evaluation of satiety was required at inclusion, and monthly after the endoscopic procedure.

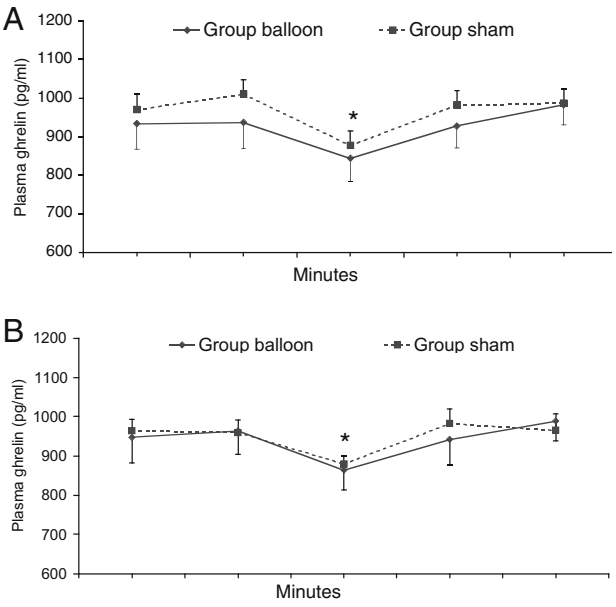

Figure 1. Plasma ghrelin levels before and after a mixed meal test in Group Balloon and Group Sham, before (Figure 1A) and 4 weeks after (Figure 1B) the intervention scheduled in each group (balloon insertion vs sham procedure). Temporal scale expressed in minutes. *P<0.05, in comparison with basal ghrelin level (-60). Data are expressed as mean±SEM.

Energy Intake

Patients were instructed to record in a structured food diary everything that they consumed for 3 days and were asked to perform food records at inclusion and 4 weeks and 4 months after the endoscopic procedures. Intakes of total energy were calculated by a single dietitian, with a computer program based on food tables (Dietsource v 1.2, Novartis).

Statistical Analysis

Data are expressed as mean ± standard deviation (if Gaussian distribution) or as median, interquartilic rank (if non-Gaussian distribution). Two-tailed parametric or non-parametric tests unpaired (Student's *t* and Mann-Whitney U, respectively) or paired (paired Student's *t* and Wilcoxon rank, respectively) tests were used when appropriate.

Multiple comparisons were analyzed by means of one-way ANOVA (for repeated measurements when indicated); post-test analysis was performed using Dunnet test. Correlations were determined by univariate linear regression (Spearman's rank test). Values for the area under the curve (AUC) for ghrelin secretion after a standard mixed meal test were calculated using the trapezoidal method. Statistical analysis was performed using SPSS 12.0 (SPSS, Chicago, IL, USA) with significance set at $P<0.05$.

Results

Subjects

During a 24-month period, 30 patients were selected according to the inclusion and exclusion criteria (23 women, 7 men). Among them, 12 patients had a positive urea breath test and completed the proton-pump-inhibitor-based triple therapy, and three of them had persistent HP infection in spite of triple therapy and were excluded. Five patients were also excluded because of one of the following: intolerance to oral endoscopy (2 patients); hiatal hernia (1 patient), or unwillingness to finish the complete follow-up (2 patients). Finally, 22 patients were included in the study protocol (17 women, 5 men; mean age 35.9 ± 9.9 years; mean BMI 50.4 ± 7.8 kg/m^2). Patient characteristics after randomization and most relevant comorbidities are reported in Table 2 and Table 3,[22] respectively. The study was completed in 21 patients; one patient in the Group A (Balloon) left the study on day 18 of follow-up because of persistent emesis.

Weight Loss and Anthropometric Variables

Pre-intervention average weight of the subjects who finished the study was 141.2 ± 27.3 kg. After 30 days of follow-up, the weight was 135.2 ± 27.1 kg ($P<0.001$). At the end of follow-up, the weight was 130.5 ± 28.4 ($P<0.001$). Among patients included in Group A (Balloon), pre-intervention average weight was 143.8 ± 31.2 kg; after 30 days of follow-up, the weight was 136.4 ± 30.9 kg ($P<0.001$) and at the end of follow-up, the weight was 131.1 ± 32.6 ($P<0.001$). Among subjects belonging to Group B (Sham), pre-intervention weight was 138.8 ± 24.5 kg; after 30 days of follow-up the weight was 134.3 ± 24.4 kg ($P<0.01$) and at the end of the study weight was 129.9 ± 25.6 ($P<0.01$). There was no significant difference between weight loss achieved in patients from Group A compared to patients from Group B at any time-point of the follow-up. Modifications of other relevant anthropometric variables are described in Table 4.

Satiety Evaluation

The pre-meal and post-meal satiety scores from Visual Analog Scale are shown in Table 5. Only patients from Group A (Balloon) showed a significant modification in the scores, which was maximal 4 weeks after the intervention. At this time-point, patients from Group A (Balloon) showed decreased hunger ($P<0.05$), decreased willingness for food ($P<0.01$) and a trend to having higher gastric fullness ($P=0.08$). However, the effect of BIB on appetite and satiety disappeared in the third month

Table 2. Patient characteristics after randomization into Group A (Balloon) and Group B (Sham)

Variables	Group A	Group B	*P*
Number of subjects	11	11	–
Gender (female : male)	8 : 3	9 : 2	ns
Age (years)*	34.8 ± 10.8	37.7 ± 8.8	ns
BMI (kg/m^2)*	49.5 ± 9.5	51.3 ± 6.1	ns
Waist circumference (cm)*	135.1 ± 15.8	133.1 ± 14.4	ns
Fat mass (%)*	48.3 ± 6.5	47.6 ± 5.2	ns
LDL-cholesterol (mg/dl)*	108.6 ± 25.0	114.5 ± 25.3	ns
HDL-cholesterol (mg/dl)*	44.6 ± 6.3	42.5 ± 12.2	ns
Triglycerides (mg/dl)†	128.0, 77	139.0, 225	ns

ns: not significant. *Expressed as mean ± SD. †Expressed as median, interquartile range.

Table 3. Patient co-morbidities after randomization into Group A (Balloon) and Group B (Sham)

Variables	Group A	Group B
DM (n / %)	3 / 27.3	4 / 36.4
Hypertension (n / %)	3 / 27.3	4 / 36.4
Dyslipidemia (n / %)	6 / 54.5	8 / 72.7
Metabolic syndrome* (n / %)	4 / 36.4	6 / 54.5
SDB (n, %)	3 / 27.3	0 / 0
Osteoarthropathy (n / %)	3 / 27.3	5 / 45.5
CHD (n / %)	1 / 9.1	0 / 0
Thyroid dysfunction (n / %)	1 / 9.1	1 / 9.1

DM, diabetes mellitus; SDB, sleep disordered breathing; CHD, coronary heart disease.
*According to the Third Report of the National Colesterol Education Program Adult Treatment Panel III.[22]

Table 4. Modification in anthropometric variables before the intervention (balloon vs sham procedure) and at the end of follow-up in each group: Group A (Balloon) and Group B (Sham)

Variables	Group A	Group B	*P*
Weight (kg)			
Initial	143.8 ± 31.2	138.8 ± 24.5	
Final	131.1 ± 32.6	129.9 ± 25.6	*ns*
Change	12.7 ± 5.6	8.9 ± 9.2	
P	<0.001	<0.001	
Weight excess (kg)			
Initial	72.4 ± 29.2	71.3 ± 19.5	
Final	59.7 ± 30.0	62.4 ± 22.8	*ns*
P	<0.001	<0.001	
BMI (kg/m^2)			
Initial	50.2 ± 9.6	51.3 ± 6.1	
Final	45.7 ± 9.7	48.2 ± 7.8	*ns*
P	<0.01	<0.01	
Waist circumference (cm)			
Initial	136.7 ± 15.7	133.1 ± 14.4	
Final	130.1 ± 20.7	129.8 ± 15.5	*ns*
P	<0.05	0.16	
Fat mass (%)			
Initial	48.3 ± 8.9	47.6 ± 5.2	
Final	45.6 ± 5.6	45.5 ± 5.2	*ns*
P	<0.01	<0.01	

post-intervention and was not evident at the end of follow-up. Concordantly, in the post-meal evaluation after a standard mixed meal, the maximal response in satiety scores was found 4 weeks after the intervention and only in patients from Group A (Balloon), who had significantly decreased willingness for food (P<0.05) and a trend to less hunger (P=0.09). No differences were detected in the post-prandial evaluation of satiety performed at 60, 90 and 120 days post-intervention in any of the groups.

Ghrelin Response

No differences were detected in fasting and post-prandial plasma ghrelin levels in the two patient groups either at basal evaluation or at 4-week evaluation. At inclusion and 4 weeks after intervention (BIB vs sham procedure), ghrelin levels reached a nadir at 60 min post-prandially in both groups (Table 6, Figure 1). In Group A (BIB), the total AUC was 3667.2±689.1 pg*ml^{-1}*240 minutes (pre-intervention) and 3737.4±663.5 pg*ml^{-1}*240 minutes (post-intervention) (P ns); in Group B (sham), the total AUC was 3847.5±436.0 pg*ml^{-1}*240 minutes (pre-intervention) and 3785.0±324.7 pg*ml^{-1}*240 minutes (post-intervention) (P ns). There was no difference between the nadir ghrelin levels in Group A and Group B subjects after mixed-meal test at any time-point. Moreover, no correlation was found between any of the satiety scores at any time-point with their comparable plasma ghrelin levels.

Leptin Levels

Fasting plasma leptin decreased from 31.9 ± 16.4 ng/ml to 22.4 ± 15.1 ng/ml in Group A (BIB, P<0.01) and from 33.7 ± 13.1 ng/ml to 25.2 ± 10.5 ng/ml in Group B (Sham, P<0.05), after 30 days of therapy. At the end of the study, plasma leptin levels decreased to 20.2 ± 12.7 ng/ml in Group A (BIB, P<0.01) and to 25.7 ± 11.7 ng/ml in Group B (Sham, P<0.05). No correlation was found between preprandial satiety scores at any time-point with their comparable plasma leptin levels.

Energy Intake

Daily caloric intake estimated from 3-day food records significantly decreased 4 weeks after intervention in both groups but was not significantly different from pre-intervention values at the end of the study. No differences were found between daily caloric intake between Group A (Balloon) and Group B (Sham) at any time-point of the evaluation. We also aimed to evaluate whether changes in ghrelin secretion had an

Table 5. Pre-meal and post-meal satiety scores according to the Visual Analog Scale used to evaluate satiety

	Group Balloon					
	Pre-intervention		Post-intervention (4 weeks)		Post-intervention (120 d)	
	PreP	PostP	PreP	PostP	PreP	PostP
ITEM 1	61.8±30.8	12.8±12.6	28.0±21.6*	1.3±3.7	43.8±26.9	7.5±10.9
ITEM 2	21.8±23.3	45.7±23.9	42.2±26.5	67.0±23.3	37.1±36.5	68.6±19.5
ITEM 3	57.9±22.9	14.2±11.6	23.2±14.4**	4.7±7.1*	56.8±21.2	10.3±13.9
	Group Sham					
	Pre-intervention		Post-intervention (4 weeks)		Post-intervention (120 d)	
	PreP	PostP	PreP	PostP	PreP	PostP
ITEM 1	42.4±24.7	15.1±19.3	34.8±22.6	8.9±1.3	57.8±34.1	19.1±27.2
ITEM 2	29.6±32.9	54.3±34.2	24.1±15.6	45.0±32.2	21.2±27.5	58.0±27.1
ITEM 3	49.7±27.3	19.2±29.0	48.3±26.3	13.9±20.7	56.6±26.7	25.3±34.2

*P<0.05, **P<0.01. PreP: preprandial; PostP: postprandial.
Intervention (balloon insertion vs sham procedure) d, days.
Satiety evaluation was performed before (preprandial) and after (postprandial) a mixed meal test.
ITEM 1: "How hungry do you feel?": "Not at all" (0 points) to "Extremely hungry" (100 points).
ITEM 2: "How full do you feel your stomach?": "Not at all" (0 points) to "Extremelly full" (100 points).
ITEM 3: "How much food would you eat?": "Nothing at all"(0 points) to "A great amount"(100 points).

Table 6. Fasting and nadir plasma ghrelin after mixed-meal test in Group A (Balloon) and Group B (Sham), before and 30 days after the intervention

	GROUP BALOON			GROUP SHAM		
	Fasting ghrelin (pg/ml)	Nadir (pg/ml)	Change from baseline (%)	Fasting ghrelin (pg/ml)	Nadir (pg/ml)	Change from baseline (%)
Pre-intervention	934.4± 199.2	844.4± 178.0**	90.0 (9.6)	970.1± 125.2	877.5± 121.6**	92.6 (9.5)
Post-intervention	947.1± 195.1	863.9± 149.1*	83.2 (8.8)	962.0± 93.9	879.1± 68.9*	84.9 (8.6)

*P<0.05, **P<0.01.
Intervention (balloon insertion vs sham procedure).

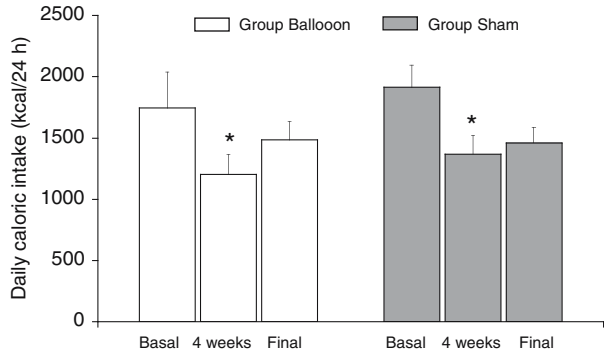

Figure 2. Estimated daily caloric intake in Group Balloon and Group Sham at basal evaluation, and 4 weeks and 120 days (final evaluation) after the intervention (balloon insertion vs sham procedure). **P*<0.05, in comparison to basal daily caloric intake. Data are expressed as mean±SEM.

impact on the reduction in caloric intake and on body weight loss. No correlation was found between post-intervention AUC of ghrelin suppression and the daily caloric intake obtained 4 weeks after the intervention in any of the groups. The estimated daily energy intake in both groups is shown in Figure 2.

Discussion

In the last decades, the use of intragastric devices has been proposed as an adjuvant therapy to induce satiety and promote weight loss in treatment-resistant obese patients, by means of a less invasive than surgery procedure. However, the first intragastric devices, such as Garren-Edwards® gastric bubbles (American-Edwards Laboratories), Ballobes® (DOT ApS) or Taylor® (Dunlop Limited) intragastric balloons had no significant effects for weight reduction in several prospective and controlled studies.[23-26] Their lack of effectiveness was attributed to the small volume, and the weak mechanical effect of air-filling and cylinder-like shape on stomach wall. In order to overcome these technical limitations, the recently introduced BioEnterics® Intragastric Balloon (BIB) has a spherical shape and is filled with a high volume of saline solution (500-700 ml). The efficacy and safety of BIB has been assessed in a number of uncontrolled studies.[3-5,7,27] Moreover, preoperative treatment of morbidly obese patients with the temporary placement of a BIB has been proposed as an adjuvant therapy for weight reduction, to decrease morbidity and mortality of surgical procedures.[8-10] However, evidence that the weight reduction after BIB placement was directly related to this device and not a placebo effect was lacking, because no randomized controlled trials had been published when this study started. Thus, we considered that the independent effect of BIB in terms of induced sense of satiety and clinical effectiveness needed to be assessed.

We tested the hypothesis that BIB-induced satiety could be mediated by suppression of pre- and/or postprandial ghrelin levels. Markedly suppressed ghrelin levels have been found after gastric bypass,[16] possibly contributing to appetite- and weight-reducing effects of this procedure. However, at the time-point of maximal satiety in our study, levels of ghrelin were not different between BIB- and sham-treated patients, suggesting that BIB-induced satiety is not mediated by modification in ghrelin levels. As described in air-mediated models,[28] acute BIB-mediated fundic distension does not appear to modify ghrelin secretion despite an efficacious induction of satiety. However, it has been reported that plasma ghrelin levels were significantly decreased 6 months after balloon insertion in spite of concomitant weight loss.[29] It is plausible that BIB effect on ghrelin secretion could be mediated by a mechanical compression and/or ischemia of the fundic mucosa which requires a longer placement. However, if 6-month BIB therapy could inhibit ghrelin secretion, this effect would not explain the impact of the balloon on satiety, as BIB-induced satiety was completely lost after our 4-month trial. Thus, in agreement with other researchers, we propose that BIB-induced satiety might be mainly caused by stimulation of the stretch receptors and a decreased stomach residual volume.[30]

Prospective uncontrolled studies reported a mean weight loss of 13.9-18.1 kg and 12.0-15.7 kg after 4- and 6-month therapy with the BIB, respectively.[3,4,6,8,30,31] Our results after 4-month follow-up are concordant with those reported before. However, the different characteristics of our study group in comparison with the previous ones (treatment-resistant obesity assessed in a multidisciplinary Obesity Unit and a higher mean BMI) could explain the slightly lower efficacy in terms of weight loss. The first randomized placebo-controlled double-blind trial in which safety and efficacy of the BIB was tested has

been recently published.[32] In this study, an independent benefit of BIB therapy could not be demonstrated, because sham- and balloon-treated groups had a similar mean weight loss of 11.2 kg and 12.9 kg, respectively during the first 3 months of therapy. Similarly, in our study, no differences in weight loss or in other anthropometric variables were found in sham- and BIB-treated patients, which is consistent with a non-dependent impact of BIB placement on energy intake that we describe. However, in a more recent double-blind, randomized, sham-controlled, crossover study, Genco et al[33] elegantly showed a significantly higher weight loss in the BIB-group than in the sham-group after 3 months of therapy before (15 kg vs 3 kg, respectively) and after crossover (13 kg vs 6 kg, respectively). In order to explain these discordances, we hypothesize that the exhaustive periodic assessment of dietetic habits included in our study, similar to the study designed by Mathus-Vliegen et al,[32] could improve the adherence of sham-treated patients and the achievement of a higher than expected weight loss.

In this study, we showed that BIB induces a significant but temporary sense of satiety in morbidly obese patients and that this effect is not mediated by modification of pre- or postprandial levels of plasma ghrelin. In spite of this, short-term placement of the BIB does not induce a clinically significant weight reduction beyond diet, exercise and behavioral therapy in treatment-resistant, obese candidates for bariatric surgery. Short and long-term effects of BIB need to be analyzed in controlled studies with a sufficient number of patients in order to assess its utility in pre-surgical management of morbid obesity.

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References

1. Bray GA, Tartaglia LA. Medicinal strategies in the treatment of obesity. Nature 2000; 404: 672-7.
2. Pereira Cunill JL, Garcia-Luna PP, Astorga Jimenez R. Pros and cons of surgery in obesity. Rev Clin Esp 2003; 203: 567-9.
3. Totte E, Hendrickx L, Pauwels M et al. Weight reduction by means of intragastric device: experience with the bioenterics intragastric balloon. Obes Surg 2001; 11: 519-23.
4. Doldi SB, Micheletto G, Perrini MN et al. Treatment of morbid obesity with intragastric balloon in association with diet. Obes Surg 2002; 12: 583-7.
5. Loffredo A, Cappuccio M, De Luca M et al. Three years experience with the new intragastric balloon, and a preoperative test for success with restrictive surgery. Obes Surg 2001; 11: 330-3.
6. Sallet JA, Marchesini JB, Paiva DS et al. Brazilian multicenter study of the intragastric balloon. Obes Surg 2004; 14: 991-8.
7. Genco A, Bruni T, Doldi SB et al. BioEnterics Intragastric Balloon: The Italian experience with 2,515 patients. Obes Surg 2005; 15: 1161-4.
8. Weiner R, Gutberlet H, Bockhorn H. Preparation of extremely obese patients for laparoscopic gastric banding by gastric-balloon therapy. Obes Surg 1999; 9: 261-4.
9. Busetto L, Segato G, De Luca M et al. Preoperative weight loss by intragastric balloon in super-obese patients treated with laparoscopic gastric banding: a case-control study. Obes Surg 2004; 14: 671-6.
10. Alfalah H, Philippe B, Ghazal F et al. Intragastric balloon for preoperative weight reduction in candidates for laparoscopic gastric bypass with massive obesity. Obes Surg 2006; 16: 147-50.
11. Kojima M, Hosoda H, Date Y et al. Ghrelin is a growth-hormone-releasing acylated peptide from stomach. Nature 1999; 402: 656-60.
12. Nakazato M, Murakami N, Date Y et al. A role for ghrelin in the central regulation of feeding. Nature 2001;409:194-8.
13. Tschop M, Smiley DL, Heiman ML. Ghrelin induces adiposity in rodents. Nature 2000; 407: 908-13.
14. Cummings DE, Purnell JQ, Frayo RS et al. A preprandial rise in plasma ghrelin levels suggests a role in initiation in humans. Diabetes 2001; 50: 1714-9.
15. Tschop M, Weyer C, Tataranni PA et al. Circulating ghrelin levels are decreased in human obesity. Diabetes 2001; 50: 707-9.
16. Cummings D, Weigle D, Frayo S et al. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. N Engl J Med 2002; 346: 1623-32.
17. Le Roux CW, Patterson M, Vincent RP et al. Postprandial plasma ghrelin is suppressed proportional to meal calorie content in normal-weight but not obese subjects. J Clin Endocrinol Metab 2005; 90: 1068-71.
18. Gastrointestinal surgery for severe obesity. National Institutes of Health Consensus Development Conference

Draft Statement. Obes Surg 1991; 1: 257-65.
19. SEEDO'2000 consensus for the evaluation of overweight and obesity and the establishment of criteria for therapeutic intervention. Sociedad Espanola para el Estudio de la Obesidad. Med Clin (Barc) 2000; 115: 587-97.
20. Romero H, Martinez-Brocca MA, Pereira JL, Garcia-Luna PP. Pharmacological treatment of obesity. Rev Esp Obes 2005; 3: 13-25.
21. Suerbaum S, Michetti P. Medical progress: Helicobacter pylori infection. N Engl J Med 2002; 347: 1175-86.
22. Executive summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486-97.
23. Benjamin SB, Maher KA, Cattau EL et al. A double-blind controlled trial of the Garren-Edwards gastric bubble: an adjunctive treatment for exogenous obesity. Gastroenterol 1988; 95: 581-8.
24. Meshkinpour H, Hsu D, Farivar S. Effect of gastric bubble as a weight reduction device: a controlled crossover study. Gastroenterol 1988; 95: 589-92.
25. Mathus-Vliegen EMH, Tytgat GNJ. Intragastric balloons for morbid obesity: results, patient tolerance and balloon life span. Br J Surg 1990; 77: 76-9.
26. Geliebter A, Melton PM, McCray RS et al. Clinical trial of silicone-rubber gastric balloon to treat obesity. Int J Obes 1991; 15: 259-66.
27. Hodson RM, Zacharoulis D, Goutzamani E et al. Managment of obesity with the new intragastric balloon. Obes Surg 2001; 11: 327-9.
28. Erdman J, Lippl F, Schusdziarra V. Differential effect of protein and fat on plasma ghrelin levels in man. Regul Pept 2003; 116: 101-7.
29. Mion F, Napoleon B, Roman S et al. Effects of intragastric balloon on gastric emptying and plasma ghrelin levels in non-morbid obese patients. Obes Surg 2005; 15: 510-6.
30. Herve J, Wahlen CH, Schaeken A et al. What becomes of patients one year after the intragastric balloon has been removed? Obes Surg 2005; 15: 864-70.
31. Doldi SB, Micheletto G, Perrini MN et al. Intragastric balloon: another option for treatment of obesity and morbid obesity. Hepatogastroenterology 2004; 51: 294-7.
32. Mathus-Vliegen EMH, Tytgat GNJ. Intragastric balloon for treatment-resistant obesity: safety, tolerance, and efficacy of 1-year balloon treatment followed by a 1-year balloon-free follow up. Gastrointest Endosc 2005;61:19-27.
33. Genco A, Cipriano M, Bacci V et al. BioEnterics® Intragastric Balloon: a short-term, double-blind, randomised, controlled, crossover study on weight reduction in morbidly obese patients. Int J Obes 2006; 30: 129-33.

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