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ORIGINAL ARTICLE

BioEnterics® Intragastric Balloon (BIB®): a short-term, double-blind, randomised, controlled, crossover study on weight reduction in morbidly obese patients

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Background: The BioEnterics® Intragastric Balloon (BIB®) System in association with restricted diet has been used for the short-term treatment of morbid obesity. Aim of this study was to evaluate the real, short term, efficacy of the BIB for weight reduction in morbidly obese patients by using a prospective, double-blind, randomised, sham-controlled, crossover study.
Methods: Patients were recruited from January 2003 to December 2003. After selection, they were randomly allocated into two groups: BIB followed by sham procedure after 3 months (Group A), and sham procedure followed by BIB after 3 months (Group B). All endoscopic procedures were performed under unconscious intravenous sedation. The BioEnterics Intragastric Balloon (Inamed Health; Santa Barbara, CA, USA) was filled by using saline (500 ml) and methylene blue (10 ml). Patients were discharged with omeprazole therapy and diet (1000 kcal). Patients were followed up weekly by a physician blinded to randomisation. In both groups mortality, complications, BMI, BMI reduction and %EWL were considered. Data were expressed as mean $\pm$ s.d., except as otherwise indicated. Statistical analysis was performed by means of Student's *t*-test, Fisher's exact test or χ^2 with Yates correction; $P<0.05$ was considered significant.
Results: A total of 32 patients were selected and entered the study (8M/24F; mean age: 36.2 $\pm$ 5.6 years, range 25–50 years; mean BMI 43.7 $\pm$ 1.5 kg/m^2, range 40–45 kg/m^2; mean %EW: 43.1 $\pm$ 13.1, range: 35–65). All patients completed the study. Mortality was absent. Complications related to endoscopy, balloon placement and removal were absent. Mean time of BIB positioning was 15 $\pm$ 2 min, range 10–20 min. After the first 3 months of the study, in Group A patients the mean BMI significantly ($P<0.001$) lowered from 43.5 $\pm$ 1.1 to 38.0 $\pm$ 2.6 kg/m^2, while in Group B patients the decrease was not significant (from 43.6 $\pm$ 1.8 to 43.1 $\pm$ 2.8 kg/m^2). The mean %EWL was significantly higher in Group A than in Group B (34.0 $\pm$ 4.8 vs 2.1 $\pm$ 1%; $P<0.001$). After crossover, at the end of the following 3 months, the BMI lowered from 38.0 $\pm$ 2.6 to 37.1 $\pm$ 3.4 kg/m^2 and from 43.1 $\pm$ 2.8 to 38.8 $\pm$ 3.1 kg/m^2 in Groups A and B, respectively.
Conclusions: The results of this study show that treatment of obese patients with BioEnterics Intragastric Balloon is a safe and effective procedure. In association with appropriate diet it is significantly effective in weight reduction when compared to sham procedure plus diet. The BIB® procedure can play a role in weight reduction in morbidly obese patients or in the preoperative treatment of bariatric patients.
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Keywords: gastric bubble; sham control; intragastric balloon; weight loss

Introduction

Obesity is the most common nutritional disorder in western countries. The relationship between morbid obesity and medical conditions such as type 2 diabetes, hypertension, and osteo-arthritis is well established.[1,2] Many approaches have been proposed for the management of morbidly obese patients, but the basic consensus is that a tailored treatment is indicated in each patient. Bariatric surgery seems to offer results better than dietary restriction alone for long-term treatment, but its morbidity and mortality are acceptable only after failure of more conservative treatments.[3,4] To reduce the risk of complications related to comorbidities, several authors have proposed the preoperative treatment of

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morbidly obese patients with the temporary placement of a BioEnterics® Intragastric Balloon (BIB) in association with restricted diet.[5–9] However, there has thus far been no evidence that the weight loss after balloon placement is directly related to this device and not a placebo effect. Aim of this study was to evaluate the real, short-term, efficacy of the BIB on weight reduction in morbidly obese patients by using a prospective, randomised double-blind, crossover, sham-controlled study.

Patients and methods

Patients

Patients were selected, in accordance to National Institutes of Health (NIH) criteria and guidelines for obesity surgery.[4] Patients were independently evaluated by a team made up of internist, dietician and psychologist for preoperative selection. Only those patients with no medical or psychological contraindications who agreed to comply with the follow-up controls were considered eligible for randomisation. Other exclusion criteria (Table 1) were: problems precluding safe endoscopy, chronic therapy with steroids, nonsteroidal anti-inflammatory drugs, anticoagulants, history of peptic ulcer, previous gastrointestinal surgery, structural abnormalities of the gastrointestinal tract (hiatal hernia >5 cm), lesions considered at risk for bleeding (i.e. Crohn's disease), pregnancy and alterations of eating pattern (sweet eaters, nibblers, binge eaters). Eating pattern alterations were evaluated according to patients interview and questionnaire. DSM IV criteria has been used for diagnosis.

Study outline

The BioEnterics® Intragastric Balloon – BIB® (Inamed Health; Santa Barbara, CA, USA) was used in this trial. A specifically designed informed consent was signed by all enrolled patients. Graphic representation of the study is

Table 1 BioEnterics intragastric balloon exclusion criteria

Oesophagitis (>2 grade)
Hiatal hernia (>5 cm)
Peptic ulcer or its previous complication
Crohn's disease
Major psychiatric disease
Disorders of alimentary pattern
Pregnancy
Previous gastrointestinal surgery
Chronic therapy with steroids, NSAID or anticoagulants
Alcohol or drug abuse
Structural abnormalities of gastrointestinal tract
Lesions with increased risk of bleeding
Severe liver disease
Any contraindication to endoscopy
Sibutramine and Orlistat treatment

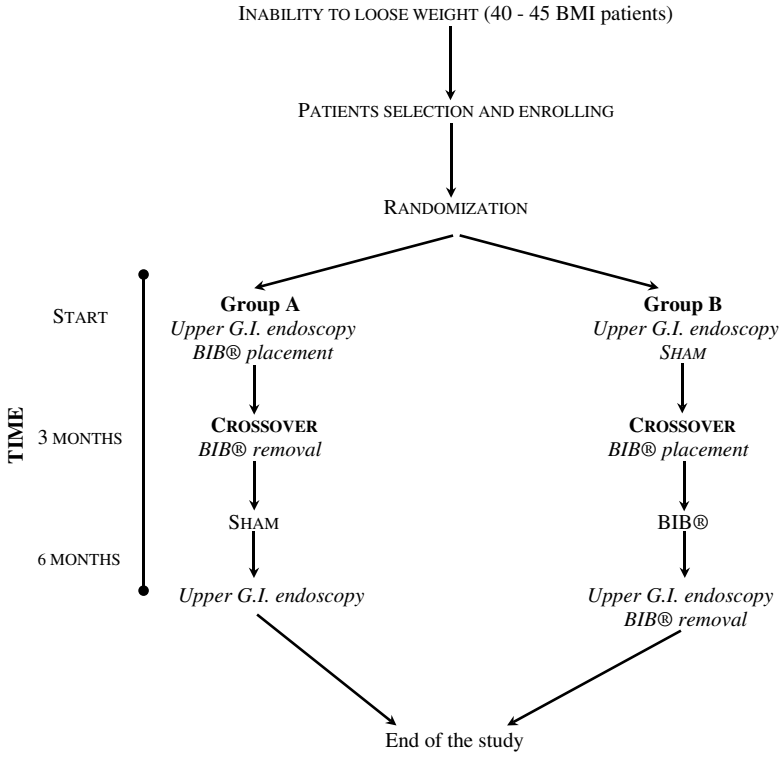

Figure 1 Study outline for the BioEnterics® Intragastric Balloon – BIB®/sham study.

reported in Figure 1. Patients were randomly allocated to their treatment by sorting a sealed envelope: Group A: 3 months BIB placement followed by 3 months sham procedure; Group B: 3 months sham procedure followed by 3 months BIB placement (Figure 2).

All procedures were performed by fully trained staff members with a previous experience of at least 50 BIB placements. After sedation (propofol: 2 mg/kg i.v.), the patient was placed in a lateral decubitus position, oesophagus, stomach and duodenum were examined, and quick test for *Helicobacter pilory* detection performed. The instrument was retrieved and the balloon was inserted into the gastric fundus. The inflation was performed under direct vision by using saline (500 ml) and methylene blue (10 ml) solution. At the end of the treatment period (3 months) in Group A patients the BIBs were removed after endoscopy, following complete deflation, with a dedicated instrument, and the removal was not followed by another balloon (sham treatment). In Group B the endoscopic examination in sedated patients was not followed by BIB insertion during the first 3 months of treatment (sham procedure). After this period the endoscopic examination was followed by BIB placement. At the end of these 3 months an endoscopy was performed in both groups.

Patients of both groups received the same medical treatment during the study. On the first postoperative day intravenous saline (30–35 ml/kg/die), omeprazole (40 mg/die), ondansetron (8 mg/die) and butylscopolamine bromide (20 mg × 3/die) were given. Patients were discharged when able to tolerate oral fluids with oral therapy: omeprazole (40 mg/die) and antiemetics if required. At day 4 after positioning, patients were instructed to begin a 1000 kcal diet (about 50% from carbohydrates, 26% from lipids and 24% from proteins, with at least 1 g proteins/kg ideal weight according to the Lorentz's formula). At 1 month after BIB placement, omeprazole was given at 20 mg/die.

Patients were weighed weekly and evaluated by a physician, blinded to patient randomisation, to assess clinical conditions. In each group, mortality, complications, BMI and %EWL were evaluated.

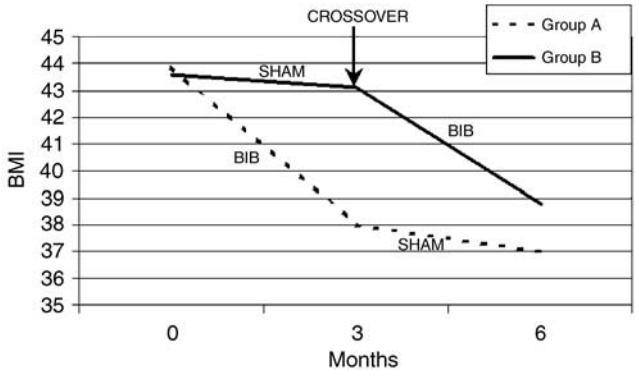

Figure 2 BMI trend during different times of the study.

Data were expressed as mean ± s.d., except as otherwise indicated. Statistical analysis was performed by means of Student's *t*-test, Fisher's exact test or χ^2 with Yates correction; $P<0.05$ was considered significant.

Results

From January 2003 to December 2003, 32 patients were selected and entered this study (8M/24F; mean age: 36.2 ± 5.6 years, range 25–50 years; mean BMI 43.7 ± 1.5 kg/m^2, range 40–45 kg/m^2; mean EW: 66 ± 9, range 49–-78 kg; mean %EW: 43.1 ± 13.1, range: 35–65). Patient characteristics after randomisation are reported in Table 2. All patients completed the study. Mortality was absent. Complications related to endoscopy, balloon placement and removal were absent. Mean time for BIB positioning was 15 ± 2 min, range 10–20 min (Group A vs B; P = NS). During the 48 h following endoscopy, several patients experienced mild abdominal pain, nausea and vomiting (Table 3). Symptoms were easily controlled by medical therapy in all cases. During the entire study period BIB was well tolerated. No gastric or oesophageal ulcer or erosion were observed. In all, 17/32 (53.12%) patients developed symptoms of gastro-oesophageal reflux, well controlled by doubling the omeprazole dosage (40 mg/die).

At the end of the first 3 months, the mean weight loss was 15 ± 6 and 3 ± 1 kg in Group A (BIB) and in Group B (sham), respectively ($P<0.001$), with a mean BMI of 38.0 ± 2.6 kg/m^2 in Group A and of 43.1 ± 2.8 kg/m^2 in Group B ($P<0.001$). The mean BMI reduction after BIB placement was higher in Group A than in Group B (5.8 ± 0.5 vs 0.4 ± 0.2 kg/m^2; $P<0.001$) (Table 4). Mean %EWL was significantly higher in Group A than in Group B patients (34.0 ± 4.8 vs 2.1 ± 1%;

Table 2 Groups A and B patient characteristics

	Group A	*Group B*
Age[a] (y)	36.2 ± 5.2; 25–50	36.3 ± 5.9; 25–50
Sex	4M/12F	4M/12F
BMI[a] (kg/m^2)	43.9 ± 1.1; 40–45	43.6 ± 1.8; 40–45
EW[a]	65 ± 11; 51–77	67 ± 9; 49–78
%EW[a]	43.5 ± 12.9; 35–65	42.9 ± 13.2; 35–65
History of obesity (months)	84 ± 11; 78–90	84 ± 12; 79–94

[a]Mean ± s.d.; range.

Table 3 Patient symptoms after the first 60 min and during the following 48 h after BIB placement or sham procedure

	Epigastric pain		*Nausea*		*Vomiting*	
	Group A	*Group B*	*Group A*	*Group B*	*Group A*	*Group B*
BIB®	13/16*	14/16	12/16	14/16	13/16	14/16
SHAM	1/16	2/16*	3/16	5/16	0/16	0/16

*$P<0.001$.

Table 4 BMI during different times of the study

	Initial BMI (kg/m^2)	*BMI loss after 3 months* (kg/m^2)	*BMI after 3 months* (kg/m^2)	*CROSSOVER*	*BMI loss 3 months after crossover* (kg/m^2)	*Final BMI* (kg/m^2)
Group A	43.9±1.1	5.8±0.5[a,*]	38.0±2.6[§]		1.1±0.3[b]	37.0±3.4
Group B	43.6±1.8	0.4±0.2[b]	43.1±2.8		5.1±0.6[a,*]	38.8±3.1

*$P<0.001$. [§]<0.001. [a]BIB®. [b]SHAM.

Table 5 %EWL during different times of the study

	Initial EW	*%EWL after 3 months*	*CROSSOVER*	*%EWL after 3 months from crossover*	*Final %EWL*
Group A	43.5±12.9	34.0±4.8[a]		4.6±1.1[b]	38.5±5.1
Group B	42.9±13.2	2.1±1[b]		31±4.8[a]	33.6±4.9

[a]BIB®. [b]SHAM.

$P<0.001$) (Table 5). However, in the 3 months following the crossover the weight loss was significantly higher in Group B (which now had BIBs) than in Group A (which had had BIBs removed) (13±8 vs 6±3; $P<0.001$). Also, mean BMI reduction was significantly higher in Group B patients during this time (5.1±0.5 vs 1.1±0.3 kg/m^2; $P<0.001$). It must be mentioned that the mean BMI reduction during the sham treatment (Figure 1) has been significantly higher in Group A than in Group B patients (1.1±0.3 vs 0.4±0.2 kg/m^2; $P<0.05$). After crossover the %EWL was significantly higher in Group B than in Group A patients (31±4.8 vs 4.6±5.1%; $P<0.001$). Also, regarding the %EWL, a significantly higher weight loss was observed during the sham period in Group A than in Group B (4.6±5.1 vs 2.1±1; $P<0.05$) (Table 5).

Discussion

The use of intragastric devices to promote weight reduction is not a novel method.[10,11] Several researchers, over the years, have used different types of balloons as they were thought to be promising as less invasive than surgery for the treatment of morbid obesity.[12–15] At the end of the 1990s several prospective and controlled studies have reported that Ballobes or Garren–Edwards gastric bubbles had no significant effects as adjuvant device for weight reduction in morbidly obese patients.[12–15] Reasons for this were considered the small volume of the balloon (220 ml for Garren–Edwards and 400 ml for Ballobes), the air filling with no weight effect on the stomach wall, and the cylinder-like shape of these devices. In addition, these devices had a high rate of complications (gastric erosion: 26%; gastric ulcer: 14%; Mallory–Weiss tears: 11%).[12–15]

The more recently introduced BIB® has a spherical shape, high volume (500–700 ml), and uses saline solution as filling. Extensive clinical experience has shown that the complication rate is very low.[5,6,8,9,15–17]

In the present study, BIB placement was safe and feasible. In all cases it was positioned after sedation only. Mortality and complications were absent. The intragastric balloon associated with proton pump inhibitors (PPIs) and antiemetics was well tolerated without any gastric or oesophageal complications such as ulcers or erosions. The main side effect was heartburn (53.12% of patients) which was well controlled by medical therapy.

As regards the effect on weight loss: this study clearly indicates that the BIB is effective as an adjuvant device for weight reduction and that its effectiveness was not a placebo effect. In the first 3 months of treatment, significantly more weight loss was observed in Group A as compared to Group B patients (Tables 4 and 5). This result can clearly be related to the presence of the intragastric balloon. The observation of weight loss in Group B patients in this period can be considered the placebo effect. After the crossover (Figure 1), the weight loss observed in Group B was significantly higher than in Group A patients (Table 4 and Table 5). During the sham period, Group A patients continued to lose weight significantly more than did Group B patients during their sham period (Table 4). This result can be considered the device effect on alimentary patients behaviour, even after its removal. How the intragastric balloon works is still unknown, although the sense of fullness and delayed gastric emptying have often been described in the literature as their chief effects.[18,20]

This study shows that the BIB® treatment is a safe and effective procedure for weight reduction. The intragastric balloon can play a role for the temporary weight reduction of morbidly obese patients in diet supporting, as well as in the preoperative treatment of patient candidate for bariatric surgery or other surgical procedures (i.e. orthopaedic prosthesis) in order to decrease morbidity and mortality.[5,6,8,19,20]

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