0016-5107/89/3505-0381$02.00
GASTROINTESTINAL ENDOSCOPY

A double-blind, randomized, sham-controlled trial of the gastric bubble for obesity

Reed B. Hogan, MD, James H. Johnston, MD
Billy W. Long, MD, James Q. Sones, MD
L. Ardell Hinton, MS, Jean Bunge, MS
Sheila A. Corrigan, PhD
Jackson, Mississippi

We investigated the effect of an endoscopically placed gastric balloon, the Garren-Edwards gastric bubble (GEGB), on weight loss in obese patients. Fifty-nine obese patients were entered into a prospective double-blind study and randomized into two groups. In one group (34 patients) the GEGB was inserted, and in the other group (25 patients) a sham insertion was done. All patients participated in a standard weight loss program consisting of dietary therapy, behavior modification, and physical exercise. The bubble was removed endoscopically after 3 months from both groups. Patients were followed for an additional 9 months after bubble removal and weight loss was monitored. Weight loss was the same in both groups at 3 months (18.7 lb vs. 17.2 lb). This was true whether determined by change in pounds, percentage of body weight, or body mass index. We concluded that the GEGB was of no added benefit as compared with sham insertion, when combined with a standard weight loss program. Because of the lack of proven efficacy and the relatively high cost, we recommend that such devices be restricted to controlled studies until significant benefits are proven. (Gastrointest Endosc 1989;35:381–385).

In 1985 the Food and Drug Administration (FDA) approved the Garren-Edwards gastric bubble (GEGB) for the treatment of obesity (Fig. 1). This intragastric balloon is a new medical device that has been in the developmental stages since the early 1970s as a free-floating intragastric balloon that is intended to serve as a "manmade bezoar."[1] The GEGB is a potentially attractive device to health care practitioners who have experienced poor results with other approaches to weight reduction.

We report the results of a randomized, double-blind, sham-controlled trail of the GEGB for the treatment of obesity. The design and methods of the trial were patterned to evaluate the benefits of the GEGB as an adjunct to a standard weight loss program (SWLP) for the short-term treatment of obesity.

Received January 29, 1988. For revision March 22, 1988. Accepted January 9, 1989.
From the St. Dominic Memorial Hospital and University Medical Center, Jackson, Mississippi. Reprint requests: Dr. Reed B. Hogan, 1421 N. State Street, Suite 203, Jackson, Mississippi 39202.

METHODS

Protocol

The main objective of the study design was to evaluate the efficacy of the GEGB when used in the manner approved by the FDA. After acceptance into the study, all patients were entered into a SWLP plus either sham or bubble placement. Three months of treatment were concluded by either bubble removal or sham removal. Following removal all patients were followed for a 9-month period of continued weight loss therapy and observed for weight loss or gain. Weight loss was recorded weekly during the period of bubble/sham placement, then biweekly over the next 3 months. Over the next 6 months, monthly meetings took place.

Enrollment of patients

The study was conducted at the St. Dominic Hospital of Jackson, Mississippi between August 1, 1986 and September 1, 1987. Approval was obtained from the Human Investigations Review Committee. Patients were solicited for participation in this study by way of two small public announcements. Of 304 initial questionnaires mailed, 160 were returned. The 160 respondents were invited to participate in an orientation session. Two orientation sessions were at-

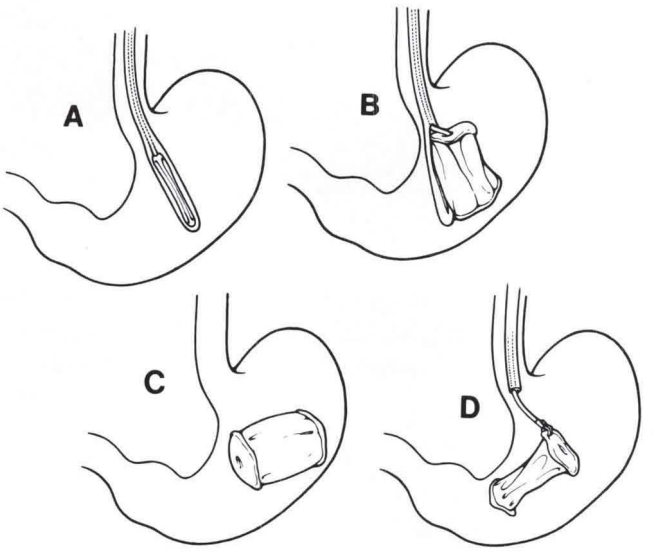

Figure 1. *A*, Insertion of overtube containing deflated bubble. *B*, Insufflation with 200 ml of air. *C*, Overtube removed, bubble left in place. *D*, Removal with endoscopic graspers after pucture and deflation.

tended by 128 subjects to initiate the process of informed consent. Those subjects willing to participate beyond that point and qualifying from the standpoint of meeting all inclusion and exclusion criteria were invited to participate (Table 1).

Using the above criteria, 59 subjects were entered into the study. They were randomly divided into four groups. Each group was assigned to one of four participating gastroenterologists who would serve as primary (blinded) physicians.

Standardized patient histories and physical examinations were obtained. All subjects were at least 50 lbs over their ideal body wt (Metropolitan Life Tables, 1979). Twenty patients (30%) were morbidly obese (100 lb [45 kg] over ideal body weight). As an incentive to adhere to the required follow-up after randomization and bubble insertion (or sham), all patients paid a $500 deposit to enter the study. This deposit was refunded at the study's end if over 80% of the follow-up appointments were met. No other charges were billed to the patients. Hospital and physician reimbursement was waived.

Assignment of patients

From a list of random numbers drawn at completion of screening endoscopy, 25 patients were randomly assigned to receive a sham endoscopy and 34 patients received GEGB placement. The stratified randomization allowed more patients to enter the balloon group, so that patients with spontaneous deflation of the bubble (a suspected frequent occurrence) could be dropped from the study without affecting analysis. Blinding was achieved by random assignment of patients to an endoscopist who was not the primary physician. Both pre- and postendoscopy care were carried out identically in all subjects.

Gastric bubble insertion versus sham

The 59 patients admitted to the study underwent endoscopy after adequate sedation using meperidine and either midazolam or diazepam (depending on the endoscopist's preference). After initial screening endoscopy was performed. If the patient still had no contraindications (Table 1), the patients were randomized to bubble placement or sham procedure while the endoscope was still inserted.

The bubble group had a GEGB inserted in the manner outlined by the manufacturer (Fig. 1). All balloons were inflated with 200 ml of air. Following removal of the introducer tube and insufflation catheter, all patients were reendoscoped to be sure of adequate placement and insufflation. Fluoroscopic guidance was used during insertion to allow for maximum safety.

The control group received a sham bubble placement. The endoscope was removed and a 48 or 50 French Maloney dilator was inserted. During this process, the procedure was mimicked as though a bubble was being inflated. After removal of the dilator, the patients were reendoscoped as we pretended to check placement, just as the balloon patients had been. At the completion of endoscopy, the patients were all treated identically as though a balloon were in place.

Standard weight loss program

The SWLP pooled the knowledge and expertise of a master's level registered dietician, master's level exercise physiologist and a PhD level clinical psychologist to formulate a 12-month eating and exercise behavior modification program. Patients were taught to plan balanced meals that were complete in all nutrients except energy. Individual intake was calculated to range from 1200 to 1800 calories, to achieve from 0.5- to 2.0-lb weight loss/week. Counseling advocated energy dilution through informed selection of high-fiber and low-fat foods. Patients were taught the exchange system rather than counting energy intake in calories. The rationale was to achieve a long-term change in eating patterns by focusing on selection from basic food groups. Exchanges provided an allowance of 0.8 to 1.2 g of protein/kg body wt, and in excess of 100 g of carbohydrates/day.

The exercise component of the SWLP involved some structured exercise participation. It was the goal of the

Table 1.
Inclusion and exclusion criteria for study

Inclusion criteria
50 lb over ideal body weight
Failure of prior dietary therapy
Informed consent
Approval of patients's regular physician
Absolute exclusions
Active peptic ulcer disease
Lesions with increased risk of bleeding
Current aspirin or nonsteroidal anti-inflammative medications
Severe liver disease
Inflammatory bowel disease
Prior gastric surgery
Structural abnormality of the upper gastrointestinal tract such as diverticulum or large hiatal hernias
Prior bowel resection
Severe cardiopulmonary disease
Psychologically unacceptable patients
Pregnancy
Any contraindication to endoscopy

exercise physiologist to strongly encourage the participants to learn to incorporate exercise into their daily routines.

RESULTS

Group characteristics

Of the 59 patients entered into the study, 56 completed the 3-month treatment portion of the protocol. Three patients in the control group were dropped from the study. Two of these dropped out the week after initial randomization because they perceived that they did not have a bubble in place. The third patient was dropped from the final analysis because his original weight recordings were invalid. Of the 56 patients completing the first 3 months, 22 were in the control group and 34 were in the bubble group. The mean age, sex, and initial weight of patients who underwent bubble placement was comparable to that of the control group. Other factors that might have influenced the outcome, such as the distance traveled from home to the weekly meetings, occupation, and so forth, did not differ significantly between groups. On admission to the study, laboratory data for the bubble group and control group did not differ significantly except that the control group had a higher incidence of hypercholesterolemia. Elevations of SGOT, fasting hyperglycemia, and hypertriglyceridemia were common (Table 2).

Compliance

During the first 3 months, subjects in the bubble group (N = 34) attended an average of 85% of all meetings; the control group (N = 22), 87%. At the conclusion of 1 year, three patients were lost to follow-up. One patient in the bubble group died. Two other patients, one in each group, moved out of state and were lost to follow-up.

Regarding the remaining patients, at the end of 1 year the bubble group (N = 32) attended 81% of the SWLP classes. The control group (N = 21) attended 78% of the classes. There was a significant dropout rate once the 3-month treatment phase was completed or once the patients had completed the required 80% of classes. At the final SWLP meeting, 28 of the initial 34 in the bubble group and 16 of the initial 22 in the sham group were present. Nine of the original 59 patients failed to meet 80% of the scheduled classes and did not receive a refund of the $500 deposit.

Table 2.
Elevation levels

	Bubble	Sham
Number	34	25
Age	33.8	36.8
M/F	6/28	5/20
Weight (lb)	246.3	239.2
Body Mass Index	39.8	37.1
Hypertension (%)	13.6	20.3
Hyperglycemia (%)	17.6	12
Elevated SGOT (%)	41	44
Elevated triglyceride (%)	47	64
Elevated cholesterol (%)	50[a]	68

[a] $p < 0.05$.

Bubble insertion

There were 34 patients randomized to receive a bubble. The time required for placement from the start of the initial endoscopy to completion of the inspection endoscopy was 12 ± 5.7 min. The inspection endoscopy in two patients revealed that the bubbles were not fully inflated. These were replaced during the same period of sedation. The sham procedures averaged 9 ± 2.1 min.

Bubble deflations

As noted above, two bubbles were not fully inflated at initial placement and were replaced. At the end of the 3-month treatment period, nine bubbles (27%) were estimated to be at least 50% deflated. Four (15%) of the bubbles were either 100% deflated or had deflated and passed spontaneously without complications (one bubble). Four bubbles (12%) were estimated to be over 50% deflated. The remaining 25 (73%) were estimated to be adequately (at least 70%) inflated. Evaluating the 25 patients in whom the bubble stayed inflated for an entire 3 months, there was no significant difference in weight loss between those patients and the control group.

Complications

During the 3 months of bubble treatment, no clinically significant complications arose. Several endoscopic findings were noted. With removal of the balloons, small tears were noted at the gastroesophageal junction in four of the balloon patients. Two patients had small gastric ulcers in the antrum. Both patients complained of dyspepsia prior to removal of the balloons. Mucosal erosions were noted in 10 subjects after balloon removal, and in two of the control group at the time of sham removal.

Several months after sham removal, one patient in the control group died from a myocardial infarction. This was viewed as an unrelated event.

Symptoms: bubble versus sham

In the first 2 weeks after bubble/sham, there was a significantly increased incidence of nausea and burning abdominal pain in the bubble patients compared with the control group. By the end of the initial 3 months, there was no significant difference in nausea, vomiting, or burning abdominal pain between the two groups (Table 3).

Table 3.
Reported symptoms

	Initial		Conclusion	
	Bubble (%)	Sham (%)	Bubble (%)	Sham (%)
Nausea	45	13[a]	24	17
Emesis	24	9	6	8
Burning pain	73	30[a]	36	33
Decreased appetite	82	74	54	54
Perceived bubble	61	30[a]	60	9[a]
Early satiety	—	—	87	39[a]

[a] $p < 0.05$.

Throughout the first 3 months, a majority of patients in both groups experienced decreased appetite. The perception that a bubble was in place was greater in the bubble group throughout the course of the study. Approximately 40% of the bubble patients felt that they did not have a bubble or were unsure. Although not measured until the final stages of the study, there was a significant increase in early satiety among the bubble patients (87%) as compared with 39% of patients in the control group (Table 3).

Weight loss results

There was no significant difference in weight loss between the groups whether measured in pounds (18.7 lb vs. 17.2 lb), percent decrease of initial body weight (7.2% vs. 8.3%), or change in body mass index (3.0 vs. 3.5; Table 4). Morbidly obese patients were evaluated separately. They were similar in respect to initial baseline parameters and their weight loss was almost identical (23 lb vs. 25 lb). When patients with greater than 50% bubble deflation were excluded from analysis (nine persons), there was still no significant difference in weight loss at 3 months (Table 5).

Long-term weight trends were difficult to follow because of the progressive dropout rate after bubble/sham removal. Evaluating weight trends in the patients who were present at the concluding meeting (bubble N = 28; sham N = 16), there was a trend of continued weight loss in the control group and weight gain in the bubble group (Table 6).

DISCUSSION

Obesity is a significant health hazard in the United States. In 1985 the National Institutes of Health consensus panel recommended weight reduction for persons more than 20% over ideal body weight.[3] Intractibility is the single most difficult characteristic in dealing with obesity. Most obese people can lose weight and have lost a great deal of it, but few maintain that loss. The "yo-yo syndrome" is characteristic of the obese.

An estimated 20 to 30 million obese persons are in the United States, including 4 to 6 million morbidly obese. Among the multitude of therapies proposed are a wide variety of diets, behavior modification techniques, exercise, multiple fad regimens, and drugs. In the population of morbidly obese patients, surgical procedures have been gaining favor (intestinal or gastric bypass, gastroplasty, etc). Surgical intervention in this group of patients is recognized to have significant morbidity and mortality.[4-7]

The use of intragastric devices for the treatment of obesity has been explored with devices other than the GEGB. Miller reported canine investigations using surgically implanted 250-ml polyethylene bottles. In that study there was no significant difference between animals implanted and the controls.[8] Other investigators have reported human investigations using a wide range of balloon sizes and materials (including "dime-store" balloons and mammary implants).[9-14]

The GEGB has been proposed as a safe, noninvasive approach to obesity. This device is intended as a temporary adjunct and the manufacturer does *not* suggest that it would be successful without concomitant diet and behavior modification. To achieve not only weight loss but permanent weight control, the GEGB has been recommended as a part of a total program involving diet counseling, exercise therapy, and behavior modification.

Table 4.
Weight loss results after 3 months of treatment

	Pounds	% weight	Body mass index
Bubbles (N = 34)	18.7	7.2	3.0
Controls (N = 22)	17.2	8.3	3.5

Table 5.
Effect of balloon deflation on weight loss at 3 months

	Study population (%)	Pounds	% weight
Total deflation (N = 5)	15	11.7	5.1
50% deflation (N = 4)	12	19.0	8.0
No deflation (N = 25)	73	19.2	7.5
Overall		18.7	7.2
Controls		17.2	8.3

Table 6.
Mean cumulative weight loss in pounds

Mo.	Bubble	Sham
3	−18.7 (N = 34)	−17.2 (N = 22)
6	−14.6 (N = 31)	−32.1 (N = 19)
9	−12.4 (N = 28)	−24.0 (N = 13)
12	−12.9 (N = 28)	−26.2 (N = 16)

The FDA approved the GEGB in 1985 for treatment of patients 20% over their ideal body weight.[15] The FDA initially recommended that the balloons be left in place for no more than 4 months. A major flaw in the initial FDA trial was the absence of a control group. All patients received the balloon and behavior modification therapy along with caloric restriction. The other concern with the FDA trial is the fact that it studied only morbidly obese patients. The study did not address the question of the bubble use in patients only 20% over ideal body weight.

Since the introduction of the device in October 1985, after 1 year, approximately one million devices had been shipped to physician customers and over 20,000 had actually been inserted. The cost is $500 per balloon with accessories plus hospital and physician charges. A recent survey suggested an average cost of up to $4,000 for a 4-month treatment.[2] The balloon can be put down by an experienced endoscopist with ease, but removal may be much more difficult. Thermal devices such as heat probes and lasers have been used to burst the balloon so that it may be deflated and retrieved.

Because of a rather high deflation rate (27% in this study), the FDA revised its initial guidelines and recommended bubble removal after 3 months of treatment. The FDA also made stricter the indications for bubble placement as the reported complications increased. Rather than 20% over ideal body weight, current recommendations include bubble placement in patients who are (1) morbidly obese, (2) with weight contributing to life-threatening conditions, (3) surgical candidates, and (4) failures at conservative therapy.[15]

The revised FDA recommendations followed the reporting of widespread complications. Complications reported in the medical literature include small bowel entrapment, gastrointestinal hemorrhage, acute pancreatitis, gastric perforation, and one death.[2, 16–19]

From the data generated in the 3-month treatment portion of this study, several conclusions can be drawn. The present GEGB did not contribute to a significant decrease in appetite as compared with a control group. Although a bubble was perceived by 60% of the bubble recipients as compared with 9% of the controls, there was no greater weight loss demonstrable in patients who either perceived the bubble or in those who claimed early satiety as compared with the rest of the bubble group.

The trend of subjects who had the bubble removed fared worse and regained some of the weight lost, whereas the sham group had a trend to continued weight loss. If valid, this would suggest an additional limitation of bubble treatment. Additionally, although clinically minor, the number of bubble-related complications in this study suggests the potential for major problems.

Recently published studies by Benjamin et al.[20] and Lindor et al.[21] have also failed to establish any significant difference between weight loss with the bubble or without it. It would appear that the present GEGB offers no additional benefits over standard weight loss therapy in the short-term treatment of obesity in motivated patients. Although the current GEGB has not been proven efficacious, it appears to be relatively safe. The concept of using a "manmade bezoar" remains an innovative and potentially efficacious approach to weight loss. The use of the bubble should be confined to controlled clinical trials until an improved design with significant benefits to the obese patient is proven.

REFERENCES

1. Garren M, Garren L, Giordano F. The Garren Gastric Bubble: an Rx for the morbidly obese. Endosc Rev 1984;1:57–60.
2. Frank BB, Stern WR, Fisher AH. Survey of gastric bubble usage in the United States, physicians workshop on the gastric bubble, 1987.
3. Hirsch J, Bell CH, Dwyer JT, Hawkins DR, Huth EJ, et al. Health implications of obesity, National Institutes of Health Consensus development Conference Statement. Ann Intern Med 1985;103:1073–7.
4. Alper DH. Surgical therapy for obesity. N Engl J Med 1983;308:1026–7.
5. Hocking MP, Duerson MC, O'Leary JP, Woodward ER. Jejunoileal bypass for morbid obesity: late followup in 100 cases. N Engl J Med 1983;308:995–9.
6. Halverson JD, Koehler RE. Gastric bypass: analysis of weight loss and factors determining success. Surgery 1981;90:446–55.
7. Andersen MD, Backer OG, Stokholm KH, Quaade F. Randomized trial of diet and gastroplasty compared with diet alone in morbid obesity. N Engl J Med 1984;310:352–6.
8. Miller JD. Intragastric prosthesis for management of obesity. World J Surg 1982;68:492–3.
9. Percival WL. "The Balloon Diet"; a non-invasive treatment for morbid obesity. Preliminary report of 108 patients. Can J Surg 1984;27:135–6.
10. Nieben OG, Harboe H. Intragastric balloon as an artificial bezoar for treatment of obesity. Lancet 1982;1:198–9.
11. Taylor TV, Pullen BR. Gastric balloons for obesity. Lancet 1982;1:750.
12. Taylor TV, Pullen BR. Initial experience with a free floating intragastric balloon in the treatment of morbid obesity. Gut 1983;T43.
13. Geliebter A, Wostreich S, Kral JG, et al. Intragastric balloon reduces spontaneous food intake and induces weight loss [Abstract]. Fed Proc 1983;42:664.
14. Henning AE. Abundant weight loss by a balloon placed in the stomach. Intern Med 1979;6:149–52.
15. FDA Drug Bulletin 1986;16:17.
16. Boyle TM, Augs SG, Bauer JJ. Small intestinal obstruction secondary to obtruation by a Garren Gastric Bubble. Am J Gastroenterol 1987;82:51–3.
17. Fleisher A, Conti PS, McCray RS, Nay HR. Jejunal entrapment of a gastric balloon. JAMA 1987;257:930.
18. Kirby DF, Mills PR, Kellum JM, Messner JM, Sugerman HJ. Incomplete small bowel obstruction by the Garren-Edwards gastric bubble necessitating surgical intervention. Am J Gastroenterol 1987;82:251–3.
19. American Edwards, Clinical letter: procedural comments on the use of the gastric bubble. October, 1985.
20. Benjamin SB, Maher KA, Cattau EL, et al. Double-blind controlled trial of the Garren-Edwards Gastric Bubble: an adjunctive treatment for exogenous obesity. Gastroenterology 1988;95:581–8.
21. Lindor KD, Hughes RW Jr, Ilstrup DM, and Jenson MD. Intragastric balloons in comparison with standard therapy for obesity—a randomized double-blind trial. Mayo Clin Proc 1987;62:992–6.