

## Effects of Intra-gastric Balloon on Weight Loss, Physical Activity, Plasma Leptin and Ghrelin in Obese Patients, with Long-Term Follow-Up

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### ABSTRACT

**AIM:** Intra-gastric balloon (IGB) represents, in the short-term, an alternative for obese patients non responding to diet and reluctant to surgery. Long-term effects of IGB have been rarely described.

**METHODS:** BioEnterics IGB were placed in consecutive patients with Body Mass Index (BMI) higher than 30 kg/m<sup>2</sup> with at least one co-morbidity, or BMI higher than 35 kg/m<sup>2</sup>. Body weight and physical activity (actimetry) were assessed before IGB insertion and just after removal. Efficacy was assessed at balloon removal (6 months), at 12 months and later on. Patients with excess weight loss (EWL) of more than 30 % were considered as responders.

**RESULTS:** Sixty-seven patients (59 women, 88%) had a balloon inserted then removed at 6 months. Mean age±SD was 38.9±9.7 years, mean BMI 36.6±3.3 kg/m<sup>2</sup>. At balloon removal, BMI

dropped to 32.2±4.0 kg/m<sup>2</sup> ( $p=0.0001$ ); 35/67 patients (52%) had EWL >30%. Energy expenditure (METS) did not change. Plasma C-peptide and leptin decreased at 6 months ( $p=0.001$ ). The ghrelin/leptin ratio increased ( $p=0.007$ ). Twenty-nine patients (43%) had a median follow-up of 53 months. Nine of these patients (31%) were still EWL responders at last visit. These long-term responders (possible selection bias) had a smaller baseline waist circumference (<110 cm) and lower plasma C-peptide levels.

**CONCLUSION:** The short-term efficacy of IGBs persisted in one third of patients after long-term follow-up, especially in those with smaller baseline waist circumference and lower plasma C-peptide levels.

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**Key words:** Intra-gastric balloon; Obesity; Weight loss; Physical activity-ghrelin; Leptin

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### INTRODUCTION

Obesity is a major cause of morbidity and mortality in developed countries. Its prevalence in several European countries exceeds 20%<sup>[1]</sup>. Treatment of obesity relies mainly on prolonged hypo-caloric diet, associated with behavioural changes, drugs or surgery. Hypo-caloric diet is the mainstay of first-line treatment, but long-term response is difficult to achieve. Surgery, mainly represented by laparoscopic adjustable gastric banding (LAGB), sleeve gastrectomy, and Roux-en-Y gastric by-pass (RYGB), markedly reduces body weight and medical complications of obesity<sup>[2,3]</sup>. However, serious complications may occur and many morbidly obese patients are reluctant to surgery. Bariatric surgery is an irreversible process. It needs a general anaesthesia. Less than 1% of obese patients fulfilling inclusion criteria for bariatric surgery actually benefit from this technique. Therefore, intra-gastric balloon (IGB) inserted by

endoscopy may represent a solution for obese patients who failed to lose weight due to non compliance or poor response to prolonged diet. Though short-term efficacy of IGB is well established<sup>[4-11]</sup>, its long-term effects have been rarely assessed. In addition, the role of hormones involved in the regulation of appetite and of metabolism is increasingly studied.

The present single-centre open-label prospective cohort study aimed to assess both short-term and long-term effects on Body Mass Index (BMI), Excess Weight Loss (EWL), physical activity (actimetry), and ghrelin and leptin plasma levels of an IGB inserted for 6 months by endoscopy in obese patients with or without co-morbidities, in conjunction with a medically supervised diet.

## METHODS

### Patients

From May 2006 to end of December 2011, 67 patients had a balloon inserted and had their weight measured both at baseline and at 6 months (just after balloon removal). During the same period, a total of 235 patients attended to a preliminary visit in view of balloon insertion. To be included, patients had to be obese men or women (BMI between 30 and 35 kg/m<sup>2</sup> with at least one co-morbidity or BMI higher than 35 kg/m<sup>2</sup> with or without co-morbidities), aged from 18 to 60 years, with a documented failure to achieve weight loss of more than 10% during at least one supervised weight loss program within two years prior to enrolment, and no history of abdominal surgery or large hiatal hernia (>5 cm) and no previous history of inflammatory diseases of the GI tract, no peptic ulcer, no oesophageal or gastrointestinal motility disorder such as gastroparesis, no ongoing treatment with a weight loss medication, or anticoagulants, or NSAIDs, a good general health status and no evidence of psychiatric disorder. Women of childbearing age had to use a contraceptive method all along the study. Proton pump inhibitors were prescribed to all patients 48 hour before insertion and until balloon withdrawal. All patients gave a written informed consent. The protocol of this study was approved by a French ethics committee (Committee for the Protection of Persons, Aulnay-sous-Bois, Seine Saint-Denis, France). This study was declared to AFSSAPS clinical trial registry (Agence Française de Sécurité Sanitaire des Aliments et Produits de Santé) (No 2005/07/021).

### Methods

The study protocol included a screening visit with assessment of physical activity (actimetry), 3-4 weeks before IGB placement and with biological assessment, then 3 follow-up visits at weeks 1, 4 and 12 after balloon insertion, then IGB removal at week 24 (6 months) with actimetry determined soon after balloon removal. At the final follow-up visit scheduled 6 months after balloon removal (12 months after its insertion), we found that many patients were lost to follow-up. Therefore, we decided to extend follow-up by inciting patients to attend to an additional follow-up visit, not scheduled by the protocol and set at a variable time when each patient could attend to the visit. Excess Weight corresponded to the difference between baseline weight and ideal weight. Ideal BMI was considered to be 25 kg/m<sup>2</sup>. % Excess Weight Loss (EWL) was obtained by dividing weight loss (in kg) by Excess Weight and multiplying the result by 100.

Systematic upper GI tract endoscopy aimed to identify any contra-indication to the placement of a BioEnterics® Intra-gastric Balloon (BIB®, ALLERGAN®, Santa Barbara, CA, USA), which was moved gently down along the oesophagus into the stomach during the same procedure. The balloon was then filled in with sterile saline. The

recommended fill in volume was 500 mL, including a small amount of methylene blue in order to facilitate the diagnosis of balloon rupture. To remove the balloon at the end of the 6-month period, a needle instrument was inserted via a gastroscope into the stomach to puncture the device.

Dietician counselling did not consist of a standardised hypocaloric regime but of personalised information adapted to individual diet. Grossly, a 1650-1800 calories/day (cal/d) diet was proposed to women, and a 2100-2200 cal/d diet to men. The protocol did not modify the amount of physical activity (and free living energy expenditure), which was assessed by actimetry by means of a wireless accelerometer SenseWear® Pro2 armband using the Professional Software version 5.0 (BodyMedia Inc., Pittsburgh, PA, USA). Durations of sleep, of physical activity, graded as sedentary, moderate, vigorous, strenuous, were registered. Subjects were instructed to wear the armband non-stop during 3 consecutive days except for one shower per day. BodyMedia SenseWear® has already been used in the field of bariatric surgery<sup>[12]</sup>.

Plasma insulin and C-peptide levels were determined by solid phase chemiluminescent immunometric assays on an Immulite® 2000 automate (DPC Siemens, Los Angeles, CA, USA). Plasma leptin, ghrelin, and GLP-1 levels were assayed in duplicate, using specific and sensitive radioimmunoassay kits from Linco Research (St-Charles, MO, USA).

### Statistical analysis

For paired comparisons of quantitative parameters, which represented the great majority of the variables studied, non-parametric Wilcoxon signed-rank tests were used, comparing for each patient the ranks of values before and either 6 or 12 months after placement of the balloon. Mann-Whitney tests were used to compare duration of sleep and of recumbent position between the patients who responded to balloon therapy and those who did not. Friedman tests were performed for repeated measures. For reasons of simplicity, results are presented as means±SD rather than medians with inter-quartile ranges. Two-tailed tests were used. *P* values<0.05 were considered as statistically significant. Bonferroni correction was used to adjust for multiple comparisons. All analyses were performed using R software version 2.14.0 (www.r-project.org). An EWL of more than 30% was considered as a clinical success, which was confronted to potential predictors (clinical and biological baseline parameters) by means of logistic regression.

## RESULTS

### Patient characteristics

The main characteristics of the 67 patients are presented in Table 1. There were 59 (88%) women and 8 (12%) men, with a mean age±SD of 38.9±9.7 years, a mean BMI of 36.6±3.3 kg/m<sup>2</sup>, a mean waist-to-hip ratio of 0.91±0.07. Concerning co-morbidities at baseline, 13 patients had hypertension, 5 had type 2 diabetes mellitus, 5 had sleep apnoea, 25 suffered from arthralgias, 11 had dyslipidemia, and 5 had hypothyroidism. Forty patients (60%) had at least one co-morbidity (21 had only one). Among baseline population, mean total calorie intake amounted to 2771±549 cal/d, and mean proportions of carbohydrates, proteins and fat were 44.2%, 17.9% and 37.1% respectively. Mean number of steps was 8997±4096. Mean baseline METS amounted to 1.19±0.21. Sleep lasted 6.2±2.5 hours, recumbent position 5±2 h, sedentary activity 13.2±3.1 h. Duration of moderate to vigorous physical activity was 0.35±0.34 h, including 0.34±0.33 h of moderate exercise.

**Table 1** Main results of the 67 patients assessed at 6 months.

Patient characteristics (units)	Number of patients with data (%)	Before balloon (baseline) Mean±SD (range)	After 6 months of balloon Mean±SD (range)	P value
Females/Males	67 (100 %)	59 women/8 men		
Age (years)	67 (100 %)	38.9±9.7 (21-60)		
Weight (kg)	67 (100 %)	98.4±12.6 (75-141)	86.6±14.3 (57-131)	0.0001
BMI (kg/m <sup>2</sup> )	67 (100 %)	36.6±3.3 (30.9-48.2)	32.2±4.0 (24.2-45.7)	0.0001
Excess Weight (%)	67 (100 %)	40.0±4.9 (28.8-54.3)	31.3±7.7 (8.6-51.9)	0.0001
WHR	35 (52 %)	0.91±0.07 (0.78-1.05)	0.88±0.08 (0.72-1.12)	0.004
% fat DEXA	33 (49 %)	49.4±4.3 (39.8-60.7)	45.7±5.6 (31.5-56)	0.0001
Fasting blood glucose (mmol/L)	9 (13 %)	5.02±0.46 (4.3-5.8)	5.16±0.35 (4.6-5.8)	0.07
Total plasma cholesterol (mmol/L)	9 (13 %)	4.67±1.85 (1.28-7.43)	5.02±2.26 (1.34-9.11)	0.10
Plasma insulin (pmol/L)	31 (46 %)	419 ± 432 (76-668)	108±104 (29-154)	0.0001
Plasma C peptide (pmol/L)	35 (52 %)	2033±1442 (194-5462)	1158±941 (311-4601)	0.001
Plasma ghrelin (pg/mL)	34 (51 %)	1393±645 (30-2720)	1285±604 (370-2800)	0.54
Plasma leptin (ng/mL)	35 (52 %)	88.8±31.8 (34-120)	60±48 (11-290)	0.0001
Ghrelin/Leptin (%)	34 (51 %)	0.18±0.11 (0.45-58.3)	0.32±0.24 (2.1-114)	0.007
Plasma GLP1 (pmol/L)	31 (46 %)	52.2±21.2 (16-98)	57.6±18.7 (22-98)	0.2

BMI: Body Mass Index; WHR: Waist-to-Hip Ratio; DEXA: Dual Energy X-ray Absorptiometry.

### Effects of intra-gastric balloon on weight loss and physical activity at 6 months

Table 1 shows the main effects of IGB placed for 6 months on weight, BMI, Excess Weight and EWL. Mean weight significantly dropped from 98.4±12.6 to 86.6±14.3 kg ( $p=0.0001$ ). Mean BMI also dropped from 36.6±3.3 to 32.2±4.0 kg/m<sup>2</sup> ( $p=0.0001$ ). Excess weight decreased from 40.0±4.9 % before balloon to 31.3±7.7% after 6 months with balloon ( $p=0.0001$ ), representing an EWL of 30.8% ±17.8%. Overall, weight decreased at 6 months in 64/67 (96%) patients. EWL assessed at 6 months was higher than or equal to 30% in 35 out of the 67 patients (52%) and higher than or equal to 20% in 49/67 patients (73%). A drop in BMI by more than 5 kg/m<sup>2</sup> was observed in 30/67 (45%) patients. Waist-to-Hip ratio significantly decreased from 0.91±0.07 to 0.88±0.08 ( $p=0.004$ ).

Forty-five patients had their physical activity assessed by actimetry both at baseline and 6 months later. Physical activity, as assessed by mean METS and number of steps, did not change (from 1.19±0.21 to 1.20±0.19 and from 9336±4257 to 9208±5001 respectively), but duration of recumbent position significantly increased from 4.53±1.34 h to 5.53±2.23 h ( $p=0.01$ ), as duration of sedentary exercise from 12.5±2.5 h to 15.5±4.3 h ( $p=0.001$ ). Duration of moderate exercise remained stable (0.34±0.34 h). Duration of vigorous and strenuous exercise remained very close to nil. Sleep duration was statistically significantly longer among responders (EWL>20%) than among non responders (6.4 h±2.4 h vs. 4.6±2.8 h;  $p=0.04$ , Mann-Whitney). Similarly, duration of awake recumbent position was significantly longer among responders (5.8±2.7 h vs. 4.1±2.5 h;  $p=0.04$ , Mann-Whitney).

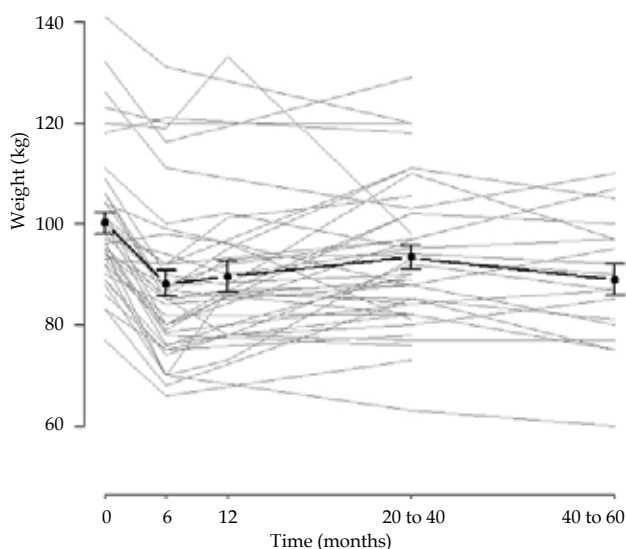
### Effects of intra-gastric balloon on weight loss long after balloon removal (Table 2)

At 12±1 months (5-7 months after balloon withdrawal), only 24 patients (36%) could be assessed. In these patients, mean body weight was 95.5 kg at baseline, dropped to 85 kg at 6 months and slightly increased to 87.5 kg at 12 months. Similarly, BMI amounted to 36.7 kg/m<sup>2</sup> at baseline, decreased to 31.9 kg/m<sup>2</sup> at 6 months ( $p=0.0001$ ) and slightly increased to 33.6 kg/m<sup>2</sup> at 12 months. EWL assessed at 12 months was higher than or equal to 30% in 8 out of the 24 patients (33%) and higher than or equal to 20% in 12/24 patients (50%). A drop in BMI higher than or equal to 5 kg/m<sup>2</sup> was observed in 6/24 (25%) patients.

Long-term follow-up (median 53 months) could be obtained in 29 patients (46%). Nine of these 29 patients (31%) had EWL of 30% or more and 14 had EWL of 20% or more (48%). A drop in BMI higher than or equal to 5 kg/m<sup>2</sup> was observed in 8/29 (28%) patients. Figure 1 shows the time evolution of individual body weights for patients who were followed up for longer than 12 months.

### Effects of intra-gastric balloon on biological parameters (Table 1)

Fasting blood glucose and plasma total cholesterol remained stable during the 6-month period of IGB. Plasma insulin and C-peptide significantly dropped at 6 months ( $p=0.001$ ). There were numerous missing data concerning biological parameters, especially blood glucose and total cholesterol. Plasma leptin significantly decreased from



**Figure 1** Changes in body weight during long-term follow-up. Individual patient data are presented in grey lines. Mean values±SD at baseline, 6 (balloon removal), 12, 20-40, and 40-60 months are presented in black bold lines.

88.8±31.8 to 60±48 ng/mL ( $n=35$ ;  $p=0.0001$ ), whereas plasma ghrelin remained stable from 1393±645 pg/mL to 1285±604 pg/mL (NS). Consequently, plasma ghrelin/leptin ratio almost doubled, from 0.18 ±0.12 to 0.32±0.24 ( $n=34$ ;  $p=0.007$ ). Plasma GLP-1 (Glucagon-Like Peptide 1;  $n=31$ ) slightly increased from 52.2±21.2 pmol/L to 57.6±18.7 pmol/L (NS).

Among the patients also assessed at 12 months ( $n=13$ ), plasma leptin significantly decreased from 70.3±31.1 ng/mL at baseline to 48±28 ng/ml at 12 months. Plasma ghrelin was stable (1599±683 pg/mL at baseline, and 1275±1302 pg/mL at 12 months). Plasma GLP-1 ( $n=14$ ) first rose from 36.1±11.1 pmol/L at baseline to 49.8±17.9 pmol/L at balloon removal ( $p=0.08$ ), then significantly dropped to 35.9±9.7 pmol/L at 12 months ( $p=0.03$  for the comparison between 6 and 12 months).

### Predictive factors for IGB efficacy

The responders to balloon therapy (EWL of 30 % or more at 6

**Table 2** Long-term results.

	Balloon insertion (baseline)	Balloon removal (6 months)	12 month follow-up (6 months after removal)	Last follow-up (median 53 months)
Weight (kg)	98.4±12.6 (n=67)	86.6±14.3 (n=67)	89±13 (n=24)	89.4±14.6 <sup>1</sup> (n=31)
BMI (kg/m <sup>2</sup> )	36.6±3.3 (n=67)	32.2±4 (n=67)	33.6±4.1 (n=24)	33.4±4.6 <sup>1</sup> (n=29)
Excess weight (%)	40±4.9 (n=67)	31.3±7.7 (n=67)	34±7.4 (n=24)	33.3±9.4 <sup>1</sup> (n=29)
Excess Weight Loss (%)	-	30.8±17.8 (n=67)	22.5±20.6 (n=24)	-
Plasma C peptide (pmol/L)	1951±1399 (n=41)	1158±941 (n=35)	1549±1489 (n=11)	-
Plasma ghrelin (pg/mL)	1393±645 (n=34)	1285±604 (n=34)	1275±1302 (n=15)	-
Plasma leptin (ng/mL)	88.8±31.8 (n=35)	60.0±47.9 (n=35)	48±28 (n=13)	-
Ghrelin/Leptin	18.2±11.6 (n=34)	31.8±24 (n=34)	35.4±32.5 (n=13)	-
Plasma GLP1 (pmol/L)	53.2±21.1 (n=33)	57.6±18.7 (n=31)	35.9±9.7 (n=14)	-

<sup>1</sup> denotes a statistically significant difference between final follow-up and baseline ( $p=0.001$ ). Seven patients were not assessed at 12±1 months according to the protocol but were assessed later on.

months) had a significantly lower waist circumference (<110 cm), lower plasma insulin and C-peptide (<1200 pmol/L) levels, and a non-significant trend to lower WHR (<0.9) at baseline (Table 3). Apart from these 4 parameters, they did not seem to have a different anthropometric or biological profile from the non responders at baseline (BMI, % EWL, WHR, calorie intake, actimetry, leptin, ghrelin, GLP-1).

**Table 3** Baseline factors predicting % EWL higher than 30%.

	Failure	Success	OR (95 % CI)	<i>p</i> -value
Age (< 35 years)	20 (62.5%)	21 (60%)	0.9 (0.34-2.41)	0.83
Male sex	6 (18.8%)	2 (5.7%)	0.26 (0.05-1.41)	0.12
BMI (< 35 kg/m <sup>2</sup> )	11 (34.4%)	9 (25.7%)	0.66 (0.23-1.89)	0.44
Waist circumference (< 114 cm)	9 (60%)	18 (90%)	6 (1-35.9)	0.05
Waist-to-Hip ratio (< 0.9)	4 (26.7%)	12 (60%)	4.12 (0.97-17.6)	0.056
C-peptide (800 pmol/L)	4 (23.5%)	14 (58.3%)	4.55 (1.14-18.2)	0.032
Plasma leptin (< 99 ng/mL)	12 (75%)	9 (47.4%)	0.3 (0.07-1.27)	0.10
Plasma ghrelin (< 1275 pg/mL)	10 (62.5%)	7 (38.9%)	0.38 (0.10-1.53)	0.17

OR means Odds Ratio, CI means confidence interval.

### Clinical tolerance of the balloon

Detailed clinical tolerance was more specifically monitored among the first 40 patients included in the study using daily reporting. Removal of the balloon at 6 months was always successful. There were 3 premature withdrawals of the balloon, 1 for psychological reasons, 1 for major weight loss, 1 for clinical intolerance. Twenty-eight patients experienced at least one adverse event (AE), representing a total of 64 AEs. AEs were predominantly moderate in severity (37 events, 66 %). The most frequent AEs were nausea (17 events, 28 %), vomiting (12 events, 19.7%), reflux (9 events, 14%), and upper abdominal pain (7 events, 10%). The majority of these AEs were device-related: 33 (54%) were definitely attributed to the device, 20 (33%) were probably related, and 3 (5%) were possibly related. A large majority of device-related AEs resolved without sequelae (47/56 events, 84%), usually within one month (43/56, 77%). Two patients experienced 5 serious device-related AEs leading to hospital stays and/or device removal. No death occurred during the study. All AEs were reported to the French National Committee for Pharmacovigilance (AFSSAPS). After this first phase, the next 27 patients were monitored for their AEs only by means of a hot line and scheduled consultations. During this latter phase, no additional serious AE was reported.

## DISCUSSION

In this open-label prospective cohort study, saline-filled IGBs installed by endoscopy for 6 months in 67 obese patients (almost

exclusively women) represented an efficient solution to treat obesity, at least temporarily. The present study is characterised by in-depth assessment of physical activity and hormone levels and provision of long-term data (median follow-up 53 months) from nearly half of the patients.

During the scheduled period of 6 months with IGB, body weight and BMI significantly dropped, leading to an Excess Weight Loss of 30.8±17.8%. At balloon removal, 35 out of the 67 patients were considered as responders since they maintained a EWL of 30% or more. This short-term effect on weight loss and BMI was quite similar to those previously described in several published series<sup>[4-11]</sup>. The finding of better results for those patients having smaller baseline waist circumference and lower plasma C-peptide is original, since usually, the higher the baseline BMI, the better the efficacy of bariatric surgery. A possible explanation might be that balloons are preferentially proposed to obese patients earlier in the course of their disease, at a stage when insulin resistance is not so prominent. This hypothesis seems strengthened by the findings of a recent article of the efficacy of intra-gastric balloons in overweight patients, showing a EWL at 3 years of 29.1% and a marked decrease in the prevalence of several co-morbidities<sup>[13]</sup>. Physical activity assessed by actimetry was unchanged, rather paradoxically in view of a major weight loss in a large proportion of patients. Actimetry provides an accurate estimate of energy expenditure when compared to indirect calorimetry and allows, using validated algorithms, to break down a person's activity into fundamental activities of walking, running, resting and sleeping. This is of particular interest since actimetry had never been performed in obese patients treated with balloon. Interestingly, durations of sleep and awake recumbent position were significantly longer among responders (EW >20 %) than among non responders. These findings might reflect the relationship between reduction of sleep and increases in energy and fat intake, with short sleep duration predisposing to obesity<sup>[14,15]</sup>. The main limitations of our study are the large amounts of missing data and of patients lost to long-term follow-up.

Data at last follow-up (median 53 months) were obtained from 29/67 (43%) of patients. Nine out of these 29 patients (31%) maintained a EWL of 30 % or more, 14/29 (50%) maintained a EWL of 20% or more, and 8/29 (28%) lost more than 5 kg/m<sup>2</sup> of BMI. These long-term results should be interpreted cautiously since patients with long-term follow-up could include a higher proportion of responders (selection bias) but are in line with those recently reported in 2 other studies. The former study showed a median EWL of 4.6 % in 41 patients evaluated at 5 years out of 99 who had a single balloon inserted for 6 months<sup>[16]</sup>. In the latter study assessing 195 patients who also completed a 60-month follow-up, BMI decreased by 2.5 kg/m<sup>2</sup> and EWL was 13%. A EWL of at least 20% was maintained in 23 % of patients<sup>[17]</sup>. The present study seems to compare favourably with both previous studies, since weight benefits



were similar even in the most pessimistic hypothesis considering all patients lost to follow-up as failures.

These results should be put in perspective with those observed after bariatric surgery. Body weight dropped by 23% 2 years after bariatric surgery, or by 25% and 17% 6 years after RYGB and LAGB respectively<sup>[18]</sup>. Weight loss was significantly higher after RYGB than after LAGB<sup>[19]</sup>. Five years after surgery, EWL amounted to 50-60%<sup>[2]</sup>. Therefore, bariatric surgery is considered the most efficacious way of losing weight for morbidly obese patients.

A decrease in insulin and C-peptide plasma levels at balloon removal (6 months) was observed in the present study, as in an Italian cohort<sup>[19]</sup>. In our study, plasma leptin significantly decreased, probably reflecting the drop in body fat, whereas plasma ghrelin remained stable, leading to an increase in the ghrelin/leptin ratio from 0.18 to 0.32. In a previous study of non-morbidly obese patients treated with a BIB<sup>®</sup> balloon, plasma levels of leptin and ghrelin significantly decreased 6 months after balloon insertion<sup>[20]</sup>. In another study of obese Caucasians receiving BIB<sup>®</sup>, plasma leptin decreased during the first 3 months after balloon placement, then remained stable during 3 months<sup>[21]</sup>. Yet another study compared subjects with a BIB<sup>®</sup> balloon placed for 6 months to 15 morbidly obese controls treated with a low-calorie diet. Plasma leptin decreased and plasma ghrelin increased by a third one month after balloon placement, then decreased reaching the starting level 3 months after removal<sup>[22]</sup>. Overall, during the 6 months with balloon, plasma leptin always decrease, whereas plasma ghrelin peaks during the first 3 months after placement then decreases. Plasma GLP-1 level was reduced in obese patients, and normalised after weight loss<sup>[23]</sup>. The present study found a non-significant trend to an increase in GLP-1 during balloon (6 months), and then a significant decrease to values close to baseline. Whereas hormone alterations seen after LAGB or intra-gastric balloon do not seem to be implied in the pathophysiology of weight loss, the rapid reduction of co-morbidities especially type II diabetes, after RYGB could be related at least partly to these alterations.

Among 50 obese patients with diet-induced weight loss (severe calorie restriction to 500-550 kcal/day for 8 weeks, followed by 2 weeks of gradual re-introduction of food), hormonal status was determined at baseline, at the end of the 10-week diet and at 62 weeks<sup>[24]</sup>. Plasma leptin decreased in parallel with weight loss, then increased in parallel with weight regain. Plasma ghrelin peaked at 10 weeks, then fell between weeks 10 and 62<sup>[25]</sup>. Plasma GLP-1 did not change from baseline to week 10, but significantly dropped from week 10 to week 62, with a final level slightly but significantly lower than baseline<sup>[25]</sup>. Thus, the evolution of hormonal parameters in our study seems more probably related to weight loss than to the presence of the balloon.

In conclusion, this study confirmed the large short-term benefit on BMI and EWL of IGBs placed for 6 months in obese patients. Rather surprisingly due to weight loss, physical activity was unchanged. The weight benefit seemed to be maintained long-term in one third of patients.

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