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Effects of Intragastric Balloon Versus Conservative Therapy on Appetite Regulatory Hormones in Obese Subjects

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ABSTRACT

Obesity is a chronic multi-factorial disease associated with serious increases in adiposity, morbidity and mortality rates. Ghrelin, leptin and adiponectin complexly interact to modulate appetite and mediate metabolic processes. The objective was to evaluate the effects of Bioenteric Intragastric Balloon (BIB) versus conservative therapy (diet and physical exercise) on plasma ghrelin, leptin, insulin and adiponectin in obese subjects. A total of 128 adult consecutive morbidly obese individuals were randomized into: BIB group comprised 84 patients treated with Intragastric Balloon and control group comprised 44 obese patients treated with conservative treatment only. In BIB group, insertion of balloon caused a significant reduction in body mass over a 6-months period compared with the control group. After one month, the levels of ghrelin increased significantly then gradually decreased, reaching the starting level three months after the removal of the balloon. Also, leptin level decreased significantly. In the control group, the corresponding of ghrelin and leptin levels remained relatively stable. In BIB group, adiponectin significantly increased as opposed to a transient increase in the control group. Conclusion: intragastric balloons in association with low-calorie diet are effective, safe, reversible, but short-lasting therapeutic endoscopic intervention in obese patients. The treatment with BIB causes significant changes in the levels of appetite-regulatory hormones beside a body mass reduction, changes in carbohydrate and lipid metabolism and improved co-morbidities.

Key words: Obesity, ghrelin, leptin, adiponectin, insulin

INTRODUCTION

Obesity is a recognized chronic multi-factorial disease associated with serious increases in adiposity, morbidity and mortality rates (Babinska *et al*., 2004). In the last decades, the prevalence of obesity is increased dramatically worldwide among variable age groups especially adults and children reaching epidemic proportions in some countries (Ogden *et al*., 2006). Obesity has become a major public health problem and one of the leading preventable causes of death and is considered the sixth most important risk factor of disease burden worldwide (Mokdad *et al*., 2004).

Obesity could be diagnosed based on body mass index (WHO, 2003). However, BMI cannot distinguish between bone, muscle and fat. Waist circumference measurement, especially if BMI is $\leq$35 kg m^{-2} could be used to track body shape changes (Green, 2009).

The excessive food energy intake and physical inactivity are believed to interpret most cases of obesity. Other possible factors which contribute to the recent increase of obesity include; genetics and environmental interactions, psychiatric illness, medications affecting appetite, endocrine disruptors interfering with lipid metabolism, infectious agents (infectobesity) and epigenetic risk factors (Bleich *et al.*, 2008; DiBaise *et al.*, 2008).

Obesity management is difficult and complex. The main accepted treatment methods of obesity include: Dietary, eating habits and lifestyle modifications, physical exercise, pharmacological, surgical and endoscopic treatment. The most physiological method of treatment is dietary modifications; however, its beneficial effect is short term and difficult to obtain (Strychar, 2006). Behavioral therapy, which includes changing lifestyle and eating habits, plays a central role in maintenance results in all obese patients independently on the method used. Pharmacological treatment options (e.g., sibutramine and orlistat) are limited and associated with multiple complications and contraindications. Bariatric surgery, an appropriate alternative approach in carefully selected individuals with severe obesity, is associated with long-term weight loss and decreased overall mortality but limited by its cost and the risk of complications (Colquitt *et al.*, 2009).

Ghrelin, leptin and adiponectin are hormones which complementary modulate appetite and mediate multiple metabolic processes. Other neuroendocrine hormonal factors which participate in mediating appetite, satiety and storage patterns of adipose tissue include: Cholecystokinin, bombesin, somatostatin, glucagon-like peptide-1 (GLP-1), obestatin, insulin, enterostatin, oxyntomodulin and peptide PYY (Flier, 2004). Cholecystokinin, peptide YY and ghrelin, influence gastrointestinal motility, modify gastric emptying causing early satiety and reduction of body weight (Cannon and Washburn, 1993).

The receptive relaxations induced by bolus deglutition and the adaptive relaxation to the increase of intragastric pressure due to food accumulation constitute gastric accommodation. Obese patients have increased gastric accommodation, which positively correlates with the volume needed to suppress food intake (Geliebter, 1988). Impairment of gastric accommodation could participate in inducing satiety and the sensation of fullness (Kindt and Tack, 2006).

Currently, the research is focused on various transoral endoluminal endoscopic techniques for treatment of obesity which are less invasive and not associated with high operative risk (Cote and Edmundowicz, 2009; Anderson *et al.*, 2008). The endoscopic modalities used include: Space-occupying devices, gastric capacity reduction methods, gastric motor function modifying methods and malabsorptive procedures. Among these techniques, only space-occupying devices with intragastric balloons are widely used (Swidnicka-Siergiejko *et al.*, 2011).

The Bioenterics Intragastric Balloon (BIB), firstly introduced in 1985 by Garren-Edwards and Taylor, has been popularly used as a safe, reversible and less invasive adjuvant approach for short-term endoscopic treatment of obesity and/or preparation of patients for bariatric surgery (Imaz *et al.*, 2008). However, the physiologic data for the BIB-induced satiety are scarce. Thus, it would be beneficial and profitable to investigate the effect of BioEnterics intragastric balloon on levels of appetite-controlling hormones such as ghrelin, leptin and adiponectin. The aim of this study is to assess the effect of BIB versus conservative therapy on appetite-controlling hormones such as ghrelin, leptin and adiponectin in morbid and non morbid obese patients.

MATERIALS AND METHODS

Subjects: A total of 138 adult consecutive outpatients, older than 20 years, with obesity; classification according to WHO criteria (WHO, 2003) were initially enrolled in this study from January 2011 through 2013.

Inclusion criteria: Obesity class 1 (BMI of 30-34.9 kg m^{-2} with severe co-morbidities; e.g., insulin-dependent diabetes), obesity class 2 (BMI of 35-39.9 kg m^{-2} without co-morbidities) and obesity class 3 (BMI of >40 kg m^{-2} as a pretreatment to bariatric surgery) were the main indications for BIB insertion. Other indications for BIB are contraindications to bariatric surgery and lack of consent for surgical treatment (Dumonceau, 2008). The study, in agreement of WMA of Helsinki declaration (WMA, 2013), was approved by the Ethical Commission and Institutional Review Board of Mansoura University Hospital in Egypt. A written informed conscious consent was obtained from all patients before their participation.

Exclusion criteria: Included advanced chronic or psychiatric illness, age <20 year, age >70 year, pregnancy, liver disease, coagulopathy, renal impairment, endocrinal and cardiopulmonary diseases, abnormal macroscopic endoscopic lesions, including gastric ulcers, cancer, hiatus hernia >3 cm, grade C or D esophagitis, or duodenal ulcers, previous gastrointestinal surgery, smokers, drug or alcohol abuse-defined as consumption of more than two alcoholic drinks per day and NSAIDs, any special type of dieting for the previous 6 months, drugs affecting appetite during the 2-4 week prior to the study, binge eaters and patients with a Body Mass Index (BMI) below 30 kg m^{-2} were excluded from the study.

Methods: Initially, all patients completed a detailed questionnaire regarding diet and habits, submitted to thorough history taking and detailed physical examinations performed at fasting in the morning. Before the study, all patients were instructed to follow a specific eating regimen; a low-calorie diet (1500 kcal day^{-1} comprised: 52.3% carbohydrates, 19.5% proteins, 28.2% lipids, 18.12 g of fiber) and physical exercise (a 45 min walk, five times a week) for one month. In specially prepared notebooks, each patient recorded the amount and type of foods eaten and checked once a month. The compliance and adherence of patients to this diet and exercise was based on their diaries. Ten patients were excluded; one binge eater, three with macroscopic endoscopic lesions, two with pregnancy and four were noncompliant (received medications affecting appetite). After one month, the remaining 128 patients were randomized and divided into two groups: the BIB (84) and control groups (44).

All the participants underwent routine investigations and upper gastrointestinal endoscopic evaluation at enrolment (a gastroscopy; XQ40, Pentax Fibreoptic, Tokyo) performed after an overnight fast between 08:00 and 10:00 a.m. to avoid the effects of diurnal hormone variation.

Group I: The BIB group: This group comprised 84 obese patients (females/males 36/48; median age 44 (29-63 years). This group was treated with the gastric balloon (Bioenteric Intragastric Balloon; BIB) for six months.

Group II: The control group: This group comprised 44 obese patients (females/males 18/26; median age 41 (32-56 years). This group continued the same conservative treatment only (dieting and physical exercise).

Bioenteric intragastric balloon: The Bioenteric Intragastric Balloon (BIB) is the most commonly used intragastric balloon (BIB, Inamed Health; Santa Barbara, USA, Fig. 1a) and is made of inert, nontoxic silicon elastomer resistant to corrosion by gastric acid forming a sphere when inflated, equipped with a self sealing radio-opaque anti-reflux valve that is connected to a

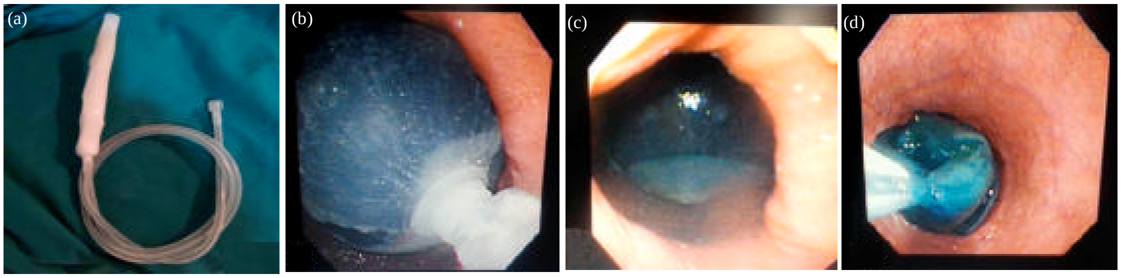

Fig. 1(a-d): (a) Bioenteric Intragastric Balloon (BIB), (b) BIB during its filling with saline and dye, (c) After filling and placement and (d) During BIB removal

catheter, rounded, soft, smooth surface without sharp borders, radio opaque, strong, water-filled and easy endoscopic insertion and removal. However, its volume is no longer adjustable (Schapiro *et al*., 1987; Galloro *et al*., 1999).

The balloon was endoscopicaly positioned in the stomach under conscious sedation or general anesthesia using propofol; 0.25 mg kg^{-1} with additional doses of 20-30 mg every 30-60 sec when necessary until the maximum dose (400 mg) plus fentanyl 50 µg in a single dose administered intravenously for its analgesic properties). The balloon, with its combined cylinder, was lubricated with xylocaine gel before insertion to facilitate its passage through the esophageal sphincters. After balloon insertion into the stomach, it was positioned and verified in the fundus under endoscopic control. Then it was filled with 500-600 mL of physiological saline containing 10 mL of methylene blue dye (Fig. 1b). The BIB was released by gentle traction of the catheter against the gastric cardia. This would allow the covering membrane to free itself gradually releasing the balloon from its constraint into the stomach. The radio-opaque anti-reflux valve prevented saline from flowing back (Fig. 1c). Monitoring all patients during the procedure with pulse oximetry, blood pressure measurement, heart rate, respiratory frequency, oxygen saturation and level of consciousness (OAAS; Observer's Assessment of Alertness Sedation Scale) (Chernik *et al*., 1990). All participants of group I (BIB group) were aware that BIB insertion is an adjuvant, temporary and short-term endoscopic method to promote weight loss. Following BIB placement, an initial liquid diet was gradually replaced with a solid diet. They were advised to follow small frequent soft meals and avoid lengthy periods in supine position. All patients were hospitalized for at least 24 h following BIB placement to observe and control any side effect including nausea, vomiting and epigastric pain.

The following visits were scheduled: The recruitment of the patients (point: -1); randomization of the subjects into two groups and BIB insertion (point: 0); one month after BIB insertion (point: 1); BIB removal 6 months after its insertion (point: 2); three months after the BIB removal (point: 3). Randomization was performed by an independent physician by sequentially opening numbered opaque envelopes with group allocation cards in a random sequence.

On each visit, the selected subjects examined for any potential complication of BIB therapy, had their anthropometric measurements, Oral Glucose Tolerance Test (OGTT), determination of fasting glucose and insulin concentration and serum levels of ghrelin, leptin and adiponectin. Abdominal X-ray was done to check the position and degree of inflation of the balloon and detection of methylene blue in urine.

Anthropometric measurements: Body: Body weight was measured with the use of a calibrated balance to the nearest 0.1 kg. Standing height was measured by a wall-mounted standiometer to the nearest 0.1 cm. Waist Circumference (WC) was measured at the superior border of the iliac crest after a normal expiration to the nearest 0.1 cm. BMI (kg m^{-2}) calculated as body weight in kilograms divided by the square of their height in meters (Weigle *et al*., 2003). The appetites of all subjects were estimated using a 100 mm Visual Analog Scale (VAS) of appetite (Flint *et al*., 2000). Start weight (SW) minus Ideal weight (IW) equals Excess weight (EW). Start weight minus Current weight (CW) equals Excess Weight Lost (EWL). Excess weight lost divided by excess weight multiplied by 100 equal Percentage Of Excess Weight Lost (PEWL) (Kim *et al*., 2008). Adult Body Fat Percentage = (1.20×BMI)+(0.23×Age)- (10.8×sex)-5.4 where sex is 1 for males and 0 for females (Deurenberg *et al*., 1991).

After a maximum of six months from BIB placement (to avoid the increased risk of spontaneous balloon deflation), the balloon was removed endoscopically also under conscious sedation with evaluation of the esophagus, stomach and duodenum searching for any potential complications caused by the BIB. All patients should be aware that the methylene blue dye (in case of balloon deflation) as well as propofol used for sedation could cause green coloration of urine. The balloon removal was done by a needle puncture then the saline was emptied through the catheter then removed using a foreign-body forceps (Fig. 1d).

Biochemical assays: A zero time (baseline) venous blood sample withdrawn from the antecubital vein at 07.00 a.m. after 12 h fasting before the beginning OGTT, centrifuged and the separated plasma was kept frozen at -70°C until assayed for ghrelin, leptin and adiponectin levels. OGTT is performed in the morning between 08.00-10.00 a.m. (to avoid diurnal variation) after an overnight fast (WHO, 1999). Blood is drawn at 0 and 2 h intervals for measurement of glucose, insulin. Urine samples may also be collected for testing along with the fasting and 2 h blood tests (for renal glycosuria).

The plasma glucose levels were measured immediately by the use of an enzymatic, colorimetric method with glucose oxidase diagnostic kit (Cormay Glucose, Lublin, Poland) using automated glucose analyzer (YSI 2300 Glucose Analyzer; YSI, Yellow Springs, OH).

Serum total cholesterol and triglycerides were determined by enzymatic methods with a chemistry analyzer (Hitachi 747, Tokyo, Japan). Low-density Lipoprotein (LDL) cholesterol was calculated using the formula of Friedewald *et al*. (1972).

All venous blood samples for hormonal assays were collected after an over-night fast into the Lavender Vacutainer tubes (VT-6450), centrifuged at 2000-3000 rpm for 15 min at 4°C and stored at -70°C until assayed. All samples for hormonal assays were performed in duplicate.

The plasma insulin, ghrelin, adiponectin and leptin were determined by ELISA kits provided from Linco/Millipore Research Inc., St. Charles, MO; Bio-manufacturing and Life Science Research. The plasma insulin was determined by ELISA kit (Catalog no. EZHI-14K). The diagnostic accuracy was 76-103% and the standard curve range was 2-200 μU mL^{-1}. The intra-assay and inter-assay coefficients of variation (CVs) were 4.6-7 and 9.1-11.4%, respectively. The data are provided by the manufacturer of the human insulin ELISA kit.

The insulin sensitivity/resistance was calculated with The Homeostasis Model Assessment (HOMA-IR, Table 1) for insulin resistance (Matthews *et al*., 1985) and the Quantitative Insulin Sensitivity Check Index (QUICKI) (Katz *et al*., 2000).

Table 1: Homeostasis model of assessment-insulin resistance (HOMA-IR) and the quantitative insulin sensitivity check index (QUICKI) formulas

Formulas	Conversion factors
HOMA-IR international formula	
Fasting glucose (mmol L^{-1})×fasting insulin(mU L^{-1})/22.5	Convert glucose mg dL^{-1} to mmol L^{-1} (Divide it by 18)
HOMA-IR US formula	
Fasting glucose (mg dL^{-1})×fasting insulin (μU mL^{-1})/405	Convert glucose mmol L^{-1} to mg dL^{-1} (Multiply it by 18)
QUICKI formula	
1/(log fasting insulin (μU mL^{-1})+log fasting glucose (mg dL^{-1}))	Convert insulin pmol L^{-1} to μU mL^{-1})/L (Divide it by 6.945)

The circulating plasma ghrelin was determined by ELISA kit (Catalog no. EZHGRA-88K). The diagnostic accuracy was 94.7-94.8%, sensitivity was 8 pg mL^{-1} and specificity was 100%. The inter-assay and intra-assay coefficients of variation (CVs) were 7.5-12.4 and 0.9-7.5%, respectively. The data are provided by the manufacturer of the human active ghrelin ELISA kit.

The plasma adiponectin level was determined by ELISA kit (Catalog no. EZHADP-61K). The diagnostic accuracy was 92-102%, sensitivity was 1.5 ng mL^{-1} and the standard curve range was 1.5-100 ng mL^{-1}. The inter-assay and intra-assay coefficients of variation (CVs) were 2.4-8.4 and 1-7.4%, respectively. The data are provided by the manufacturer of the human adiponectin ELISA kit.

The plasma leptin level was determined by ELISA kit (Catalog no. EZHL-80K). The diagnostic accuracy was 94-114%, sensitivity was 0.5 ng mL^{-1} and the standard curve range was 0.5-100 ng mL^{-1}. The inter-assay and intra-assay coefficients of variation (CVs) were 2.6-6.2 and 2.6-4.6%, respectively. The data are provided by the manufacturer of the human leptin ELISA kit.

Statistical analysis: Data were analyzed using SPSS software (Version 17.0). Quantitative data were expressed as (Mean±SD) while qualitative data were expressed as number and percentage. Continuous data are expressed as median (range) and were evaluated by appropriate statistical tests; t test (for paired data e.g., plasma hormonal levels measured before and after BIB treatment). Proportions were compared by means of Fisher's exact test. Correlations were evaluated using the Spearman rank correlation coefficient test. Kruskal-Wallis One Way Analysis Of Variance (ANOVA) compares more than two groups.

Multiple regression analysis was used to assess the effects of BIB insertion on plasma ghrelin, leptin and adiponectin levels, adjusted by the body mass change. Subgroups (percentages of patients) were compared by using the McNemar test. A value of $p<0.05$ was considered statistically significant. Sensitivity, specificity and predictive values were calculated to study the overall predictability of other techniques.

RESULTS

Ten patients of a total of 138 adult consecutive outpatients with obesity from the study were excluded according to exclusion criteria. The remaining 128 patients were randomized and divided into two groups: The BIB (84) and control groups (44). BIB was removed in three patients due to unbearable complications (gastric ulcer, GIT bleeding). Two patients from control group underwent bariatric surgery (Table 2).

Both groups did not differ significantly ($p>0.05$) as regard to age, sex, clinical, laboratory and anthropometric data (Table 3). Also, there were no significant differences within the same age or sex group as regard baseline clinical, demographic, laboratory and anthropometric data. There were no significant correlations between clinical, demographic, laboratory and anthropometric data at the start of the study in both groups.

Table 2: Flow chart of the study

Parameters (n(♀/♂))	A total of 138 consecutive adult outpatients with obesity Ten patients were excluded according to exclusion criteria Remaining 128 (54/74) patients were assigned to the following groups Treatment BIB group (84 (36/48))	Control group (44(18/26))
Baseline at BIB insertion	84 (36/48)	44 (18/26)
After one month	81(35/46) (BIB was removed in three patients due to un-tolerable complications)	42 (17/25) (two patients underwent surgical treatment)
After 3 months	80 (34/46) (one received drugs which affect appetite)	41(17/24) (one received drugs which affect appetite)
After 6 months	80 (34/46)	40 (17/23) (one lost in followup)

Table 3: Baseline characteristics in the studied groups (BIB and control)

Parameters	BIB (84)	Control (44)	p-value
	------------------------------Mean±SD	---------------------------	
Age (y; median(min-max))	44 (29-63)	41 (32-56)	0.349
(y; M±SD)	43.960±8.980	42.65±6.610	
Sex (F/M: 54/74)	0.571±0.490	0.59±0.497	0.834
Height (m)	1.690±0.040	1.71±0.050	0.142
B. weight (kg)	136.900±7.970	137.80±9.800	0.615
Body Mass Index (BMI)	47.870±1.080	47.46±1.850	0.180
Body Fat Percentage (BFP)	55.990±5.650	54.98±5.750	0.347
Waist circumference (cm)	140.200±5.320	138.10±9.500	0.168
Visual Analogue Scale (VAS)	69.820±6.780	71.24±5.790	0.216
Excess Weight (EW) (kg)	65.450±5.040	65.23±6.770	0.830
Fasting glucose conc. (mg dL^{-1})	160.200±14.20	161.40±12.30	0.624
2 hPP glucose conc. (mg dL^{-1})	187.200±16.60	189.20±14.20	0.465
Fasting insulin conc. (μIU mL^{-1})	58.830±4.760	59.64±4.050	0.312
2 hPP insulin conc.(μ IU mL^{-1})	100.750±6.930	101.76±7.560	0.462
HOMA-IR	23.440±3.930	23.91±3.320	0.496
Total cholesterol (mg dL^{-1})	264.300±14.60	267.10±10.70	0.296
Low Density Lipoprotein (LDL)	70.820±10.80	68.17±10.90	0.194

After a maximum of six months from BIB placement (to avoid the increased risk of spontaneous balloon deflation), the balloon was removed endoscopicaly under conscious sedation with evaluation of upper GIT searching for any potential complications caused by the BIB. No serious complications (ulcers and bleeding) were observed except in three patients (3.5%) in whom the BIB was removed. The most common complaints after BIB placement were discomfort (47.6%), nausea (77.4%), vomiting (35.7%), bleaching (69.1%), halitosis (20.2%), flatulence (26.1%), reflux symptoms (8.3%) and no complications (35.7%).

The endoscopic application of the BIB in obese individuals caused a significant decrease in fasting and 2hPP glucose and insulin levels (Table 4). Also, insulin resistance expressed by HOMA-IR significantly improved ($p \leq 0.001$). Most of the decrease in glucose or insulin concentrations and in HOMA-IR occurred after one month of BIB insertion. Also, their concentrations and HOMA-IR continued to decrease significantly during the three months after BIB removal. On the other hand, conservative treatment in the control group did not change neither insulin level nor insulin resistance indicated by HOMA-IR ($p>0.05$). There was only a transient fluctuation in fasting and 2hPP glucose and insulin levels in the course of study in control group.

Table 4: OGTT and HOMA-IR in studied groups at different points of followup period (data expressed as Mean±SD)

Group	Timing	Fasting glucose conc.	2 hPP glucose conc. (mg dL^{-1})	Fasting insulin conc. (mIU mL^{-1})	2 hPP insulin conc.	HOMA-IR
BIB	At BIB insertion	160.20±14.30	187.20±16.70	58.8±4.760	100.7±6.93	23.4±3.93
	1 month after insertion	142.98±14.90	166.60±17.79	52.5±7.480	85.3±15.4	18.6±3.66
	At BIB removal	125.40±12.30	156.60±17.14	44.8±8.830	75.8±15.1	13.8±3.21
	3 month after removal	115.10±10.70	136.50±14.40	40.7±8.020	80.8±13.7	11.5±2.70
	ANOVA	0.0001	0.0001	0.0001	0.0001	0.0001
Control	At BIB insertion	161.40±12.23	189.29±14.20	59.6±4.050	101.7±7.5	23.9±3.32
	1 month after insertion	158.70±16.90	188.50±20.20	61.3±9.490	102.6±6.3	24.1±4.86
	At BIB removal	162.40±18.40	187.20±15.30	62.4±10.50	102.1±6.8	25.2±6.12
	3 month after removal	158.60±16.10	185.81±12.70	62.04±11.1	104.3±5.3	24.4±5.93
	ANOVA	0.590	0.752	0.49	0.246	0.634

Table 5: Anthropometric data in studied groups at different points of followup period (data expressed as Mean±SD)

Group	Timing	B.wt. (kg)	BMI	Body fat (%)	Waist circ. (cm)	EWL (kg)	PEWL
BIB	At BIB insertion	136.94±7.97	47.87±1.1	55.99±5.65	140.23±5.3	-	-
	1 month after insertion	131.45±7.90	45.96±1.6	53.69±6.07	130.11±5.8	5.54±3.150	8.4±4.550
	At BIB removal	122.65±12.6	42.92±4.2	50.05±7.10	120.98±5.6	14.33±11.37	21.5±16.75
	3 month after removal	118.77±10.7	41.57±3.7	48.43±6.98	123.50±14.3	18.20±11.63	27.3±16.90
	ANOVA	0.000	0.000	0.000	0.000	0.000	0.000
Control	At BIB insertion	137.80±9.80	47.46±1.9	54.98±5.75	138.07±9.5	-	-
	1 month after insertion	134.55±8.91	47.16±2.8	54.60±5.770	137.95±7.7	3.30±2.90	0.49±16.8
	At BIB removal	131.41±8.54	46.25±3.7	53.54±7.66	135.1±9.22	6.40±5.87	4.20±21.50
	3 month after removal	131.83±7.82	45.99±3.8	53.22±7.67	136.4±12.9	5.98±4.65	5.30±21.90
	ANOVA	0.002	0.090	0.562	0.430	0.001	0.001

PEWL: Percentage of excess weight loss

The endoscopic insertion of BIB in obese individuals caused a significant improvement of anthropometric parameters as indicated by a considerable body weight, BMI and Waist circumference reductions within 6 months-period (Table 5). In BIB group, the Excess Weight Loss (EWL) was significant (5.49±3.78 and 14.28±13.34 at 1 month and 6 months periods, respectively; $p \leq 0.001$) compared with insignificant changes in the control group (1.15±9.87 and 3.74±13.27 at 1 month and 6 months periods respectively; $p > 0.05$). The greatest EWL occurred after one month of BIB insertion. Body weight reduction continued to decrease significantly during the three months after BIB removal (18.17±11.77 $p \leq 0.001$) and still statistically significantly higher in the BIB group ($p \leq 0.001$).

The changes of appetite regulatory hormones were shown in Table 6. The plasma ghrelin levels increased significantly after one months of BIB insertion in BIB group ($p \leq 0.05$) then gradually decrease to reach its baseline values three months after BIB removal (so the overall ghrelin change with BIB insertion is not significant; ANOVA = 0. 288) while in the control group, there was only small non significant fluctuations in its level (ANOVA = 0.855). On the other hand, there was significant decrease of leptin level and significant increase of adiponectin level in BIB group (ANOVA≤0.001) compared with control group (ANOVA>0.05) throughout the observation periods. Moreover, most of the change in both hormonal levels occurred within one months of BIB insertion.

The comparison of BIB and Control groups at different points of followup period and also, comparison of the changes occurred throughout multiple visits of followup period in each group were shown in Table 7. As regard the age, sex, height, starting weight, ideal weight and excess weight, there were non-significant differences between the two groups neither at baseline nor at

Table 6: Hormonal values in studied groups at different points of followup period (data expressed as Mean±SD)

		BIB group			Control group		
		Ghrelin	Leptin	Adiponectin	Ghrelin	Leptin	Adiponectin
At BIB insertion	M	771.020	72.8230	19.200480	767.110	68.680	19.1670
	SD	32.347	26.4680	1.345864	28.451	28.550	0.7293
1 month after insertion	M	786.130	49.4880	24.471300	765.340	69.430	20.0850
	SD	31.118	25.4700	3.412400	30.210	27.850	3.4692
At BIB removal	M	78525.000	30.9110	26.840000	762.110	69.590	2.0550
	SD	86.890	20.8630	4.140100	28.451	28.790	4.5519
3 month after removal	M	772.750	26.1850	23.643000	763.310	67.390	19.3690
	SD	86.890	19.3810	3.120400	28.008	28.830	0.9022
ANOVA		0.288	0.0001	0.000100	0.855	0.983	0.3340

Table 7: Comparison of BIB and control groups and comparison of the changes occurred in each group at different points of followup period

BIB and control groups	P0 (baseline)	P1 (at one month)	P2 (at BIB removal)	P3 (at 3 month after BIB removal)	ANOVA1 (BIB group)	ANOVA2 (control)
Age (year)	0.349	0.349	0.349	0.349	1.000	1.000
Sex (F/M)	0.834	0.834	0.834	0.834	1.000	1.000
Height (m)	0.142	0.142	0.142	0.142	1.000	1.000
Body Weight (BW, kg)	0.615	0.053	0.000	0.000	0.000	0.002
Body Mass Index (BMI)	0.180	0.012	0.000	0.000	0.000	0.090
Body Fat Percentage (BFP)	0.347	0.398	0.014	0.001	0.000	0.562
Waist Circumference (cm)	0.168	0.000	0.000	0.000	0.000	0.430
Visual Analogue Scale (VAS)	0.216	0.000	0.000	0.000	0.000	0.294
Excess Weight Loss (EWL)	-	0.000	0.000	0.000	0.000	0.000
Percentage of excess weight loss (PEWL)	-	0.000	0.000	0.000	0.000	0.000
Plasma ghrelin level (pg mL^{-1})	0.484	0.000	0.028	0.365	0.288	0.855
Plasma leptin level (ng mL^{-1})	0.427	0.000	0.000	0.000	0.000	0.983
Plasma adiponectin level (ng mL^{-1})	0.858	0.000	0.000	0.000	0.000	0.334
Fasting glucose conc. (mg dL^{-1})	0.624	0.000	0.000	0.000	0.000	0.591
2hPP glucose conc. (mg dL^{-1})	0.465	0.000	0.000	0.000	0.000	0.752
Fasting insulin conc. (mIU mL^{-1})	0.312	0.000	0.000	0.000	0.000	0.494
2hPP insulin conc. (mIU mL^{-1})	0.462	0.000	0.000	0.000	0.000	0.246
HOMA-IR index	0.496	0.000	0.000	0.000	0.000	0.635

p-value: Compares variables in BIB and control groups at different points of followup period, ANOVA: Compares the change between multiple visits of followup period in each group, ANOVA1: BIB group and ANOVA2: Control group, Significant if $p\leq 0.05$, Non-significant if $p>0.05$

any time of followup (P0, P1, P2, P3>0.05). Also, there were non-significant changes of these parameters during the followup period (from baseline upto 3 months after BIB removal) in each group (ANOVA1 and ANOVA2>0.05). On the other hand, statistically significant differences between the two groups were observed at one months, at BIB removal and three months after BIB removal (P1, P2, P3≤0.05) regarding anthropometric parameters (B. wt, BMI, Waist circ., VAS, EWL, PEWL), HOMA-IR, OGTT and insulin levels. Also, there was a highly statistically significant change of these parameters during the followup period (from baseline upto 3 months after BIB removal) in the BIB group only (ANOVA1≤0.05). While, in the control group, there was insignificant change of anthropometric parameters, OGTT, insulin and HOMA-IR during the followup period (from baseline upto 3 months after BIB removal) (ANOVA2>0.05).

As regard the plasma levels of leptin, there was a non significant difference between the two groups at baseline (p0>0.05) but there was a statistically significant difference between the two groups at one month of insertion, at BIB removal and at 3 months after BIB removal (P1, P2, P3≤0.05) being decreased in the BIB group. Also, there was a significant decrease of leptin during the followup period (from baseline upto 3 months after BIB removal) in BIB group (ANOVA1≤0.05) a finding not observed in the control group in which there was a transient non significant change in leptin level throughout the observation period (ANOVA2>0.05).

As regard the plasma levels of adiponectin, there was a non significant difference between the two groups at baseline (p>0.05) but there was a statistically significant difference between the two groups at one month of insertion, at BIB removal and at 3 months after BIB removal (P1, P2, P3≤0.05) being increased in the BIB group. Also, there was a significant increase of adiponectin during the followup period (from baseline upto 3 months after BIB removal) in BIB group (ANOVA1≤0.05) a finding not observed in the control group in which there was a transient non significant increase in adiponectin level throughout the observation period (ANOVA2>0.05).

As regard the plasma ghrelin levels, there was a non significant difference between the two groups at baseline and 3 months after removal of BIB (P0, P3>0.05) but there was statistically significant difference between the two groups at one month of insertion and at BIB removal (P1, P2≤0.05) being increased in the BIB group. Although, there was a significant increase of ghrelin level after one month of BIB insertion in BIB group, it decreased gradually to reach its baseline values at 3 months after BIB removal (ANOVA1>0.05). In the control group, there was a non significant decrease of ghrelin during the followup period (from baseline upto 3 months after BIB removal) (ANOVA2>0.05). In the BIB group, most of the changes in anthropometric parameters, hormonal, OGTT, insulin levels and HOMA-IR occurred after one month of BIB insertion (p1≤0.05).

Table 8 shows spearman rank correlation coefficient test between excess weight loss and plasma hormone levels and HOMA-IR index in both groups at baseline, at one month and after removal of BIB. In BIB group, age and sex were not correllated with neither plasma hormonal levels (ghrelin, leptin, adiponectin, insulin and HOMA-IR) nor anthropometric parameters (BMI, EWL and PEWL). BMI, BFP and body weight were statistically significantly correllated with waist circumference, EWL and PEWL. EWL and PEWL were correllated with plasma hormonal levels of ghrelin, leptin, adiponectin, insulin and HOMA-IR. A significantly negative correlations was

Table 8: Correlations between excess weight loss and plasma hormone levels and HOMA-IR index in both groups at baseline, at one month and after removal of BIB

		BIB group at			Control group at		
Parameters		Baseline	One month	BIB removal	Baseline	One month	BIB removal
Ghrelin	r	0.184	0.827	0.087	0.194	0.197	0.167
	p	0.092	0.001	0.430	0.079	0.382	0.482
HOMA-IR	r	-0.147	-0.227	-0.315	-0.029	-0.178	-0.089
	p	0.179	0.043	0.004	0.735	0.247	0.642
Leptin	r	-0.176	-0.648	-0.805	-0.012	-0.115	-0.105
	p	0.107	0.000	0.001	0.590	0.457	0.497
Adiponectin	r	-0.140	-0.336	-0.423	-0.097	-0.097	-0.187
	p	0.201	0.002	0.001	0.379	0.379	0.379

r: Spearman rank correlation coefficient test

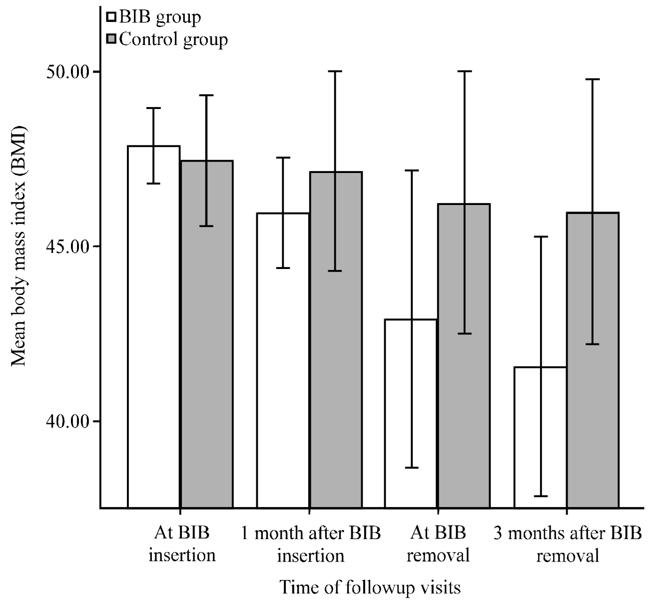

Fig. 2: Mean body mass index in the studied groups at different points of followup period

observed between leptin and excess weight loss after one and six months of BIB insertion ($r = -0.648$, $p \le 0.001$; $r = -0.805$, $p \le 0.001$, respectively). Also, there was a significantly negative correlation between adiponectin and excess weight loss after one and six months of BIB insertion ($r = -0.336$, $p \le 0.002$; $r = -0.423$, $p \le 0.001$, respectively). Ghrelin was statistically significantly correllated with leptin, adiponectin and fasting glucose, fasting insulin and HOMA-IR levels. It was significantly positively correlated with excess weight loss only after one month of BIB insertion ($r = 0.827$, $p \le 0.01$) but not at six months ($r = 0.087$, $p \le 0.430$). There was a significantly negative correlation between HOMA-IR and excess weight loss after one and six months of BIB insertion ($r = -0.227$, $p \le 0.05$; $r = -0.315$, $p \le 0.01$, respectively). Similar correlations were not observed in the control group. At baseline in both groups, plasma ghrelin, leptin, adiponectin levels and HOMA-IR were not significantly correlated with age, sex, anthropometric measurements ($p>0.05$).

There was statistically significant decrease of body mass index in BIB group throughout the observation period most of which occurred in first month after BIB insertion (Fig. 2) while in control group, there was a non significant small decrease of body mass index. There was statistically significant body weight reduction in BIB group compared with a non significant small decrease of body weight in control group. Also, there was statistically significant decrease of waist circumference in BIB group throughout the observation period despite a transitroy non significant change in control subjects.

Body fat percentage statistically significantly decreased in BIB group throughout the followup period (Fig. 3) while in control group, there was a non significant change of body fat percentage.

In this study, there was statistically significant increase of excess weight loss in BIB group throughout the followup period most of which occurred in first month after BIB insertion (Fig. 4) while in control group, there was a non significant increase of excess weight loss.

Percentage of excess weight loss statistically significantly decreased in BIB group throughout the followup period mainly in first month after BIB insertion (Fig. 5) while in control group, there was a non significant increase of PEWL.

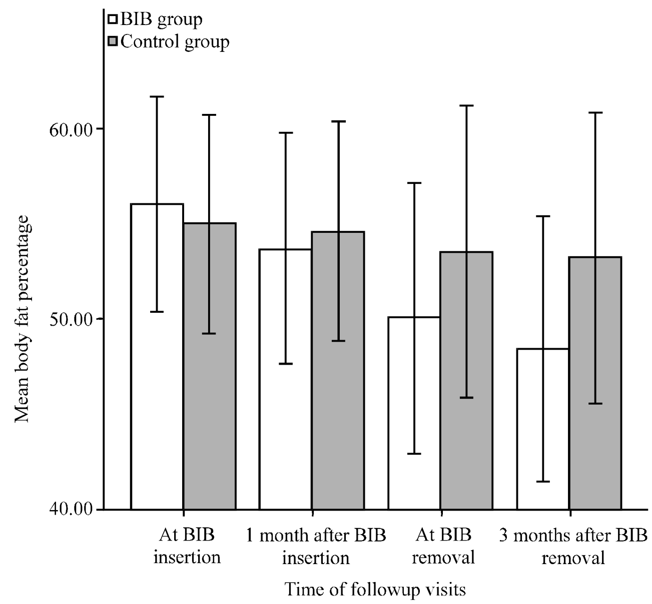

Fig. 3: Mean body fat percentage in the studied groups at different points of followup period

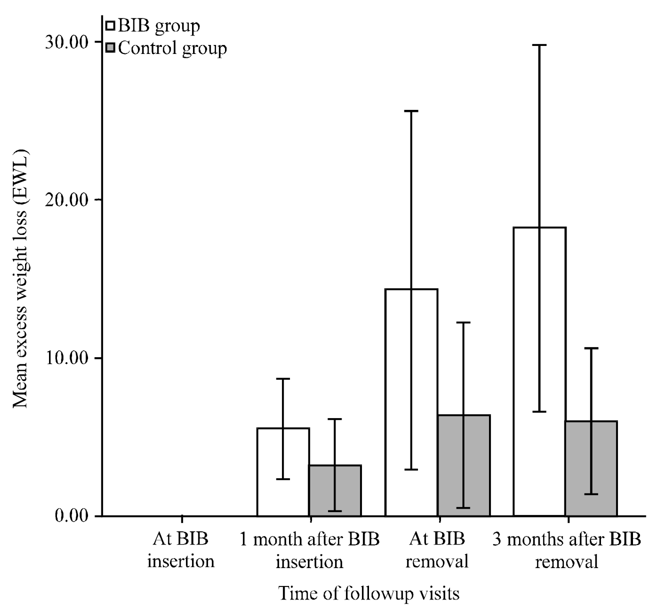

Fig. 4: Mean excess weight loss in the studied groups at different points of followup period

As regard plasma ghrelin level, there was statistically significant increase of plasma ghrelin level in BIB group within one month after BIB insertion then gradualy decrease to reach the baseline levels within three months after BIB removal (Fig. 6), while in control group, there was a non significant change of plasma ghrelin level.

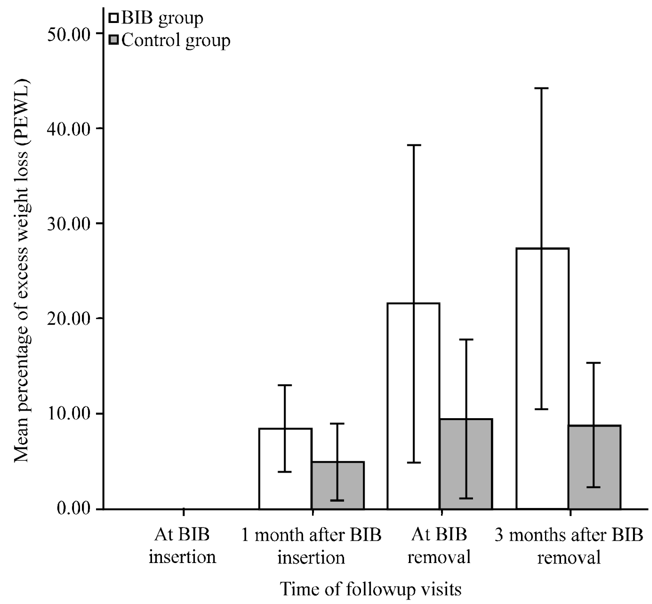

Fig. 5: Mean percentage of excess weight loss in the studied groups at different points of followup period

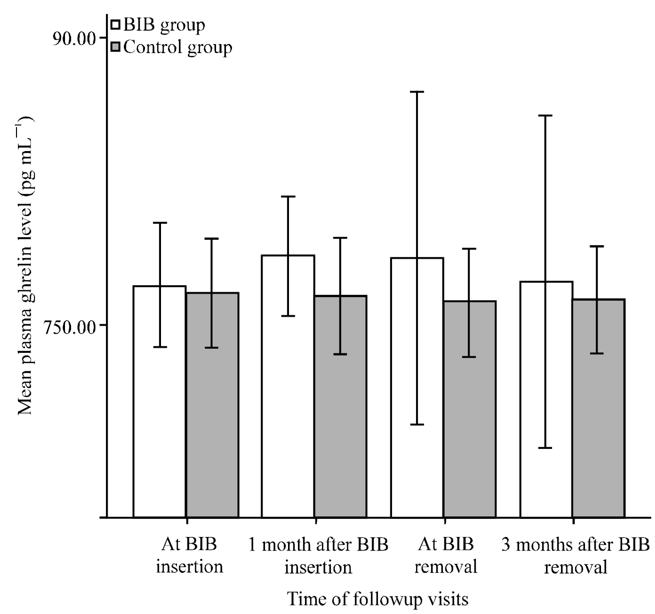

Fig. 6: Mean plasma ghrelin level in the studied groups at different points of followup period

Plasma leptin level in BIB group was statistically significantly decreased throughout the followup period especialy within the first month after BIB insertion (Fig. 7) while in control group, there was a non significant fluctuations of plasma leptin level.

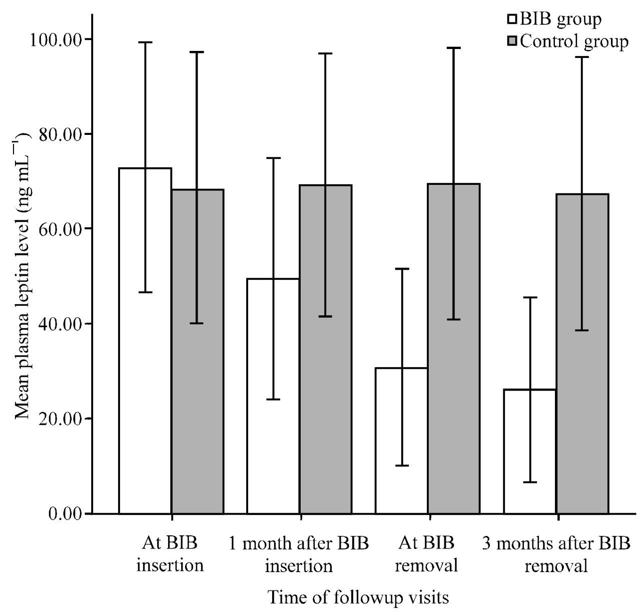

Fig. 7: Mean plasma leptin level in the studied groups at different points of followup period

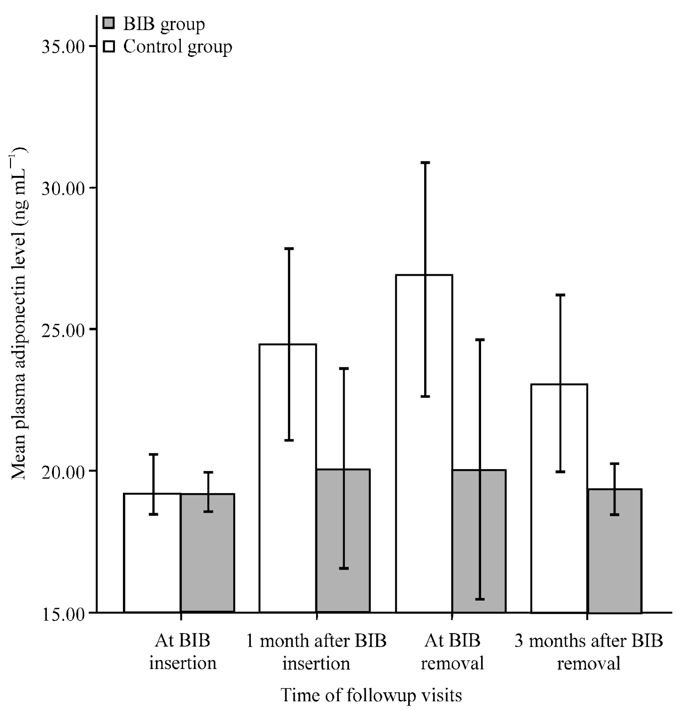

Fig. 8: Mean plasma adiponectin level in the studied groups at different points of followup period

Contrary to leptin, plasma adiponectin level statistically significantly increased in BIB group throughout the followup period mainly in first month after BIB insertion (Fig. 8) while in control group, there was a non significant fluctuations of plasma adiponectin level.

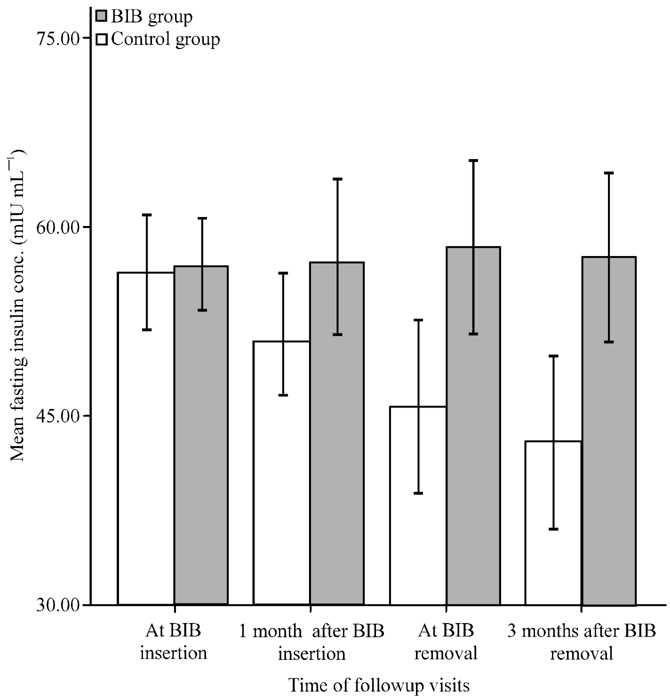

Fig. 9: Mean fasting insulin concentrations in the studied groups at different points of followup period

There was statistically significant decrease of fasting insulin concentrations in BIB group throughout the followup period most of this decrease occurred after one month of BIB insertion (Fig. 9) while in control group, there was a non significant increase of fasting insulin concentrations.

Similarly, a statistically significant decrease of HOMA-IR index (improvement of insulin resistance) was observed in BIB group throughout the followup period most of which occurred during the first month after BIB insertion (Fig. 10) while in control group, there was a non significant change of HOMA-IR index.

DISCUSSION

It is believed that obesity, a multi-factorial true pandemic chronic health disease, is increased dramatically worldwide among variable age groups, associated with serious and dramatic increases in adiposity, morbidity and mortality rates, diagnosed based on body mass index and even the modest reduction of 10% of excess body weight significantly reduces obesity-associated co-morbidities (Evans and DeLegge, 2011).

Excessive food intake, sedentary life and physical inactivity contribute to most cases of obesity. Other possible contributing factors include; endocrine factors interfering with lipid metabolism, genetics and environmental interactions, psychiatric illness, medications increasing appetite, insufficient sleep, assortative mating, natural selection for higher BMI, infectious agents (infectobesity) and epigenetic risk factors (Bleich *et al*., 2008; DiBaise *et al*., 2008).

Obesity has become a major public health problem because of its prevalence, costs and health effects. It is a well established risk factor for and associated with different chronic and metabolic disorders including: Hypertension, endothelial dysfunction, atherosclerosis, ischemic heart diseases,

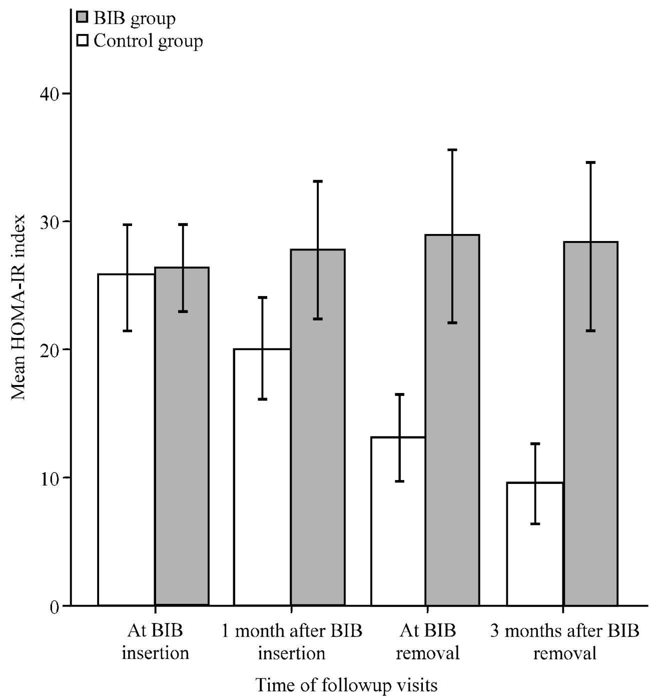

Fig. 10: Mean HOMA-IR index in the studied groups at different points of followup period

dyslipidemia, brain stroke, certain types of cancers; esophageal or colonic adenocarcinoma (El-Serag, 2005), arthritis, obstructive sleep apnea, polycystic ovary, type 2 diabetes, non alcoholic fatty liver disease (NAFLD), non alcoholic steatohepatitis (NASH) and insulin resistance syndromes. The average life expectancy is also diminished (Haslam and James, 2005).

Different treatment modalities were accepted for obesity management including: Dietary and lifestyle modifications, physical exercise and pharmacological, surgical and endoscopic treatment. Dietary modification which is considered a physiological method of treatment seldom gives durable results in the long term (Strychar, 2006). Behavioral therapy, which includes changing lifestyle and eating habits, plays a crucial role in long term results in all obese patients independently on the method used. Pharmacological treatments (e.g., sibutramine and orlistat) are limited and associated with multiple complications and contraindications.

Bariatric surgery, an appropriate alternative approach in carefully selected individuals with severe obesity, is associated with durable long-term weight loss that is sustainable for at least 10 years, decreased overall mortality and improvements in most obesity-associated co-morbidities. Of special interest, bariatric surgery could acheive diabetes curing independently of weight loss. Insulin resistance decreases within one week following Roux-en-Y gastric bypass (RYGB) surgery (Wickremesekera *et al*., 2005). In a recent randomized controlled study, the laparoscopic adjustable gastric banding (LAGB) was more effective in curing type 2 diabetes than medical therapy (Dixon *et al*., 2008). However, bariatric surgery is limited by its cost and the significant high risk of complications (Evans and DeLegge, 2011).

Currently, the research is focused toward minimally invasive trans-oral endoluminal endoscopic techniques for management of obesity. Endoluminal therapies are safe, short, reversible avoiding commitment or permanent surgical modification, reproducible endoscopic procedures, could be extended to obese with multiple co-morbidities, older age and those with mild obesity

(BMI 30-35 kg m^{-2}) and have the potential to be performed under moderate sedation. Currently, several such transoral endoluminal procedures are under investigation in the United States (Cote and Edmundowicz, 2009). The endoscopic modalities used include: Space-occupying devices, gastric capacity reduction methods, gastric motor function modifying methods and malabsorptive (duodenojejunal bypass sleeve) procedures (Cote and Edmundowicz, 2009). Among of these techniques, only space-occupying devices with intragastric balloons are widely used (Swidnicka-Siergiejko *et al*., 2011).

Most studies on endoscopic techniques for obesity, report percentage of excess weight loss (PEWL). After much research and focus on the expert guidelines, the BioEnteric intragastric balloon was introduced in 1999. It has been popularly used as a safe, reversible and less invasive adjuvant approach for short-term endoscopic treatment of obesity and/or preparation of patients for bariatric surgery (Imaz *et al*., 2008). Placement of an intragastric balloon results in complex interactions of neurohormonal factors, changes in gastric motility and the obvious space-occupying effect.

In this study, the BIB placement in the stomach for at least 6 months caused a statistically significant reduction in body weight and other anthropometric measurements (the Excess Weight Loss (EWL) was significant (5.54±3.15 and 14.33±11.37 kg at 1 month and 6 months, respectively). Three months after the removal of the balloons, the reduction in body weight and other anthropometric measurements became slowly and the final body mass reduction was lower. Although the difference was still significant when compared with the baseline values, the difference was not significant when compared with their values at BIB removal.

Similar results were obtained by other studies (Evans and Scott, 2001). A multicenter study in Brazil assessing the effect of BIB treatment on obesity showed the mean body mass reduction of 15.2±10.5 kg, 6 months after a treatment with balloons (Sallet *et al*., 2004). In a 12-month long observation of patients after endoscopic treatment with BIB introduced by (Herve *et al*., 2005), the mean body mass reduction was 12 and 8.6 kg just after and a year after the BIB removal, respectively.

On the other hand, in a study performed by (Ganesh *et al*., 2007), they demonstrated that BIB treatment has a less effective impact on body weight reduction, about 5.9 kg after 6 months of therapy and 1.9 kg after a year. However, these results might be explained by a smaller initial BMI (31.5 kg m^{-2}), smaller balloon volume (450 mL) and lack of a concomitant treatment with diet and physical exercise.

Patients with a greater initial body weight and BMI showed better response after BIB treatment (Doldi *et al*., 2002). Martinez-Brocca *et al*. (2007) showed that the mean body weight loss in the balloon and sham groups in morbidly obese subjects were similar. Whereas, (Genco *et al*., 2006) demonstrated a higher weight loss after the BIB treatment compared with the sham group.

The results of (Genco *et al*., 2006) are consistent with the results obtained in the current study. Also, the pre-insertion BMI significantly affects EWL (the higher initial BMI, the higher weight loss after the BIB treatment)

Induction of gastric satiety is complex, multi-factorial and mediated by endocrine/paracrine as well as motor functions of the stomach; the gastric distension, accommodation and emptying (Ello-Martin *et al*., 2005). Ghrelin, leptin and insulin are such hormones which complementary modulate appetite maintaining energy balance and mediate multiple metabolic processes. The effect of gastric balloons on hormonal regulation in obese patients was previously assessed but with few available reports.

Ghrelin has been demonstrated to plays central as well as peripheral roles in food intake, appetite, eating behavior, energy homeostasis, body weight regulation, gastric motility and acid secretion (Nakazato *et al.*, 2001).

Although, ghrelin has a potential role in short-terms hunger signals, its chronic administration increases body weight, moreover endogenous ghrelin levels fluctuate with body weight changes (Tschop *et al.*, 2001; Cummings *et al.*, 2002). Elevated ghrelin levels were observed in humans and other animals with weight loss achieved through a variety of methods, including food restrictions or deprivation and illness- induced anorexia (Williams and Cummings, 2005).

It is not known whether the elevation in ghrelin levels under these circumstances is a reflection of the reduced feeding or not. In a study conducted by (Leidy *et al.*, 2004), ghrelin levels increased only in the weight loss group.

The results obtained in the current study affirm these results. At the end of this intervention, the BIB group had lost a large amount of weight compared with the control group and ghrelin levels increased significantly in relation to the amount of weight lost compared with the control group. Collectively these results could demonstrate that in the absence of reduced food intake, plasma ghrelin increases in response to Excess Weight Lost (EWL) per se.

Ghrelin, an orexigenic peptide, is a major hormone stimulating appetite. Ghrelin is paradoxically decreased in obese patients but these lower levels could represent an adaptive phenomenon to reduce appetite. In the current study, the levels of ghrelin, leptin and adiponectin did not differ significantly between the groups at the baseline (at recruitment).

As regard the plasma ghrelin levels, although there was a significant increase of ghrelin level after one month of BIB insertion in BIB group, it decreased gradually to reach its baseline values at 3 months after BIB removal (ANOVA1>0.05). In the control group, there was a non significant decrease of ghrelin during the followup period (from baseline upto 3 months after BIB removal) (ANOVA2>0.05). In the BIB group, most of the changes in anthropometric parameters, hormonal, OGTT, insulin levels and HOMA-IR occurred after one month of BIB insertion ($p \le 0.05$).

In a study conducted on non-morbidly obese patients, the insertion of air-filled balloon resulted in an increase in plasma ghrelin level and a marked reduction of body weight. The plasma ghrelin increased significantly one month after the balloon insertion and returned to the initial level four months after the placement of the air balloon (Mion *et al.*, 2007). In the present study, a similar rise was observed in plasma ghrelin one month after the BIB insertion but decreased to its initial levels three months after the BIB removal. This difference in time might be due to the longer duration of BIB placement in current study (6 months vs. 4 months) with longer stimulation of the gastric wall. The mechanical stimulation of gastric wall by balloon contact could probably be responsible for the increased ghrelin in the first few months after BIB placement. Also, the increased plasma ghrelin level is probably related to negative caloric balance during the first month or an adaptive phenomenon to increase a drive to eat. However, the VAS of appetite was significantly decreased during BIB insertion and in experimental studies; the extension of the gastric wall by direct water delivery to the stomach did not affect ghrelin concentration (Williams *et al.*, 2005).

Some studies revealed that the BIB-induced satiety was not mediated by a modification in the ghrelin levels (Martinez-Brocca *et al.*, 2007). This could be due to the measurement of total ghrelin and the inactive form of this peptide.

Given the fact that circulating ghrelin contribute to body weight regulation, it would be of great interest to note that the changes in adiposity signals, leptin and insulin are complexly interplayed and involved in ghrelin regulation. There is evidence that insulin may mediate some effects of obesity on plasma ghrelin levels. In this study, ghrelin levels were compared in morbidly obese patients according to insulin sensitivity indicated by HOMA-IR. As expected for their BMI, the high HOMA-IR group had a low plasma ghrelin levels.

Ghrelin was significantly positively correlated with excess weight loss and percentage of excess weight loss only after one month of BIB insertion ($r = 0.827$, $p \le 0.01$) but not at six months ($r = 0.087$, $p \le 0.430$). There was a significantly negative correlation between HOMA-IR and excess weight loss after one and six months of BIB insertion ($r = -0.227$, $p \le 0.05$; $r = -0.315$, $p \le 0.01$, respectively).

These data support the hypothesis that the high insulin levels seen in insulin-resistant individuals (HOMA-IR) may act to reduce plasma ghrelin (insulin-resistant state may mediate the ghrelin reduction).

As regard the plasma levels of leptin, there was a non significant difference between the two groups at baseline ($p > 0.05$) but there was a statistically significant difference between the two groups at one month of insertion, at BIB removal and at 3 months after BIB removal ($p \le 0.05$) being decreased in the BIB group. Also, there was a significant reduction of serum leptin during the followup period (from baseline upto 3 months after BIB removal) in BIB group (ANOVA1$\le$0.05) a finding not observed in the control group in which there was a transient non significant increase in the level of leptin throughout the observation period (ANOVA2>0.05).

Leptin, an anorexigenic hormone, inhibits both the secretion of gastric ghrelin (orexigenic) and the appetite stimulation by ghrelin (Kalra *et al*., 2005). The endoscopic application of BIB in obese individuals in our study caused a significant improvement of anthropometric parameters as indicated by a considerable body weight, BMI, Body Fat Percentage (BFP) and Waist circumference reductions within 6 months-period. The decrease in the amount of adipose tissue resulted in a decrease of serum leptin level. This is consistent with previous studies in which the leptin reduction was observed after reduction of body mass index and body fat percentage due to bariatric surgery or diet modifications (Faraj *et al*., 2003).

Adiponectin, an adipokine mediator produced by adipose tissue, plays a crucial role in the regulating adiposity and glucose and lipid metabolism. This appetite modulating peptide reciprocally and complexly interacts with leptin and ghrelin for the development and maintenance of obesity (Fauci *et al*., 2008).

Few data on the effect of BIB on adiponectin level have been reported and the available studies refer to conservative treatment or bariatric surgery. Some authors observed an increase in the adiponectin level after a body mass reduction in surgically treated extremely obese subjects (Faraj *et al*., 2003). Others showed that despite a body mass reduction due to physical effort, the level of adiponectin remained unchanged (Ryan *et al*., 2003).

The level of adiponectin was found to be decreased in obese subjects and body weight reduction obtained after conservative, endoscopic BIB insertion or surgical treatment caused its elevation (Bacha *et al*., 2004).

Similarly, in this study, a significant reduction in body mass index in the BIB group was associated with significant increase in serum adiponectin level compared with a transitory increase in its level in the control group. In another study conducted by Konopko-Zubrzycka *et al*. (2009), they observed no changes in serum adiponectin level in spite of the significant reduction in body mass index in the BIB group. By contrast, in the control group, a transient increase in adiponectin level was noted after two months of conservative treatment. The increase in serum adiponectin was thought to be related to the way of losing weight and the beneficial influence of exercise on serum adiponectin.

Obesity by itself, especially childhood obesity, enhances and even could initiate inflammatory conditions in vessels, endothelial dysfunction and atherosclerosis (Ciccone *et al*., 2011).

Adiponectin was found, in this study, to decrease in obese individuals and significantly increased after body mass reduction induced by BIB insertion. Also, in the current study, adpionectin was significantly correllated with ghrelin, leptin, fasting glucose, fasting insulin and HOMA-IR levels. It is interesting to note that the body mass index and body fat percentage reductions in the BIB group, with simultaneous improvement in insulin sensitivity, caused significant increase in adiponectin level. In the control group, a mild decrease in body mass, with no visible effect in OGTT or HOMA-IR parameters, was associated with a transient rise in serum adiponectin level. The transient adiponectin increase in the control group could be related to a body mass reduction (1.1 kg after one month). The subsequent months of treatment with diet and physical effort turned out to be of limited effectiveness in terms of body mass reduction and consequently, in the subsequent months, adiponectin returned to the initial values.

These results affirm those obtained by Bacha *et al*. (2004) who noted that the increase in adiponectin level was found to be a prognostic factor of insulin sensitivity improvement, based on the HOMA index.

Taken collectively, we could hypothesize that adiponectin, through modulating the oxidative stress existed in obesity, could ameliorate the atherosclerotic process and improve the metabolic profile in obesity (antiatherogenic and insulin sensitizing polypeptide).

The current study has its limitations as patients' self-evaluation and the limited monitoring of the conservative treatment. All the patients completed history and questionnaire forms concerning the recommended diet and physical exercise. However, the patients' self-evaluation was not always reliable. Obese subjects frequently understate the amounts and type of food they eat. A larger control group could help to enrich a future study and perhaps verify our results.

CONCLUSION

Intragastric balloons (BIB) in association with low-calorie diet are effective, safe, reversible, well tolerated and valid but short-lasting therapeutic endoscopic intervention in patients with morbid obesity. The treatment with BIB causes significant changes in the levels of energy metabolism and appetite-regulatory hormones. This method, beside a body mass reduction in obese subjects and the accompanying changes in carbohydrate and lipid metabolism, altered the level of adiponectin and improved co-morbidities. Patient compliance with lifestyle changes and diet and the appropriate patient selection are the key pillars for optimal results. The BIB removal results in a body weight gain and impairment of insulin, carbohydrate and lipid metabolism. Another BIB insertion after the first BIB removal could be tried in future studies.

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