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Changes In Leptin Level After Different Bariatric Procedures: Gastric Balloon And Sleeve Gastrectomy, And Its Relation To The Effectiveness Of Weight Loss.

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Abstract

Background: Obesity can affect the neuroendocrine system in various ways, either by hormonal elevation as in ghrelin and growth hormone or by depression as in the case of leptin and insulin. Leptin has been previously researched in its relation to the energy homeostasis in obesity, however the effect of various surgical procedures are far from being fully understood.

Methods: A prospective multicenter case control study was done including twenty non morbidly obese (≤ 40 kg/m^2) and morbidly obese (> 40 kg/m^2)patients treated with IGB (control) or SG with base line and follow up after six months leptin level determination and weight loss assessment.

Results: Leptin showed a highly significant (P<0.001) decrease six months after the insertion of the balloon. The mean decline of leptin hormone level was 8 ug/l (+/- 5.06). In the group of sleeve gastrectomy (SG), leptin showed a significant (P<0.05) decrease six months after the operation. The mean decline of leptin hormone level was 17.6 ug/l (+/- 17.06). There was a statistically significant difference between the two groups as regard the weight loss (P<0.05).

Conclusion: The effect of different intervention procedures on the neuroendocrine system can give us an important clue to the future of individualized therapy either in the further selection of patients to undertake the most beneficial cost effective procedure or to add adjuvant hormonal therapy to the treatment.

Keywords: *leptin, sleeve gastrectomy, intragastric balloon, obesity.*

Introduction

Multiple hormones have been linked to energy balance; gherlin, pancreatic polypeptide, oxyntomodulin, peptide YY, glucagon like peptide-1, insulin, cholecystokinin, and leptin[1, 2]. Leptin might affect other hormones like influencing the circulating gherlin level [3]. In a previous study done it was shown that the dietary weight loss causes an increase in the circulatory levels of gherlin and growth hormone while decreasing the levels of leptin and insulin [4].

Leptin receptors have been categorized into four isoforms, where the long isoform of leptin receptor is mainly in the hypothalamus controlling neuroendocrine activity[5]. Obesity induces a type of leptin resistance, where the high levels of the circulating hormone does not induce satiety or reduction of adipose tissue[6].

Both intragastric balloon IGB and laparoscopic sleeve gastrectomy LSG have proven their efficacy in the treatment of obesity[7, 8].While IGB is a non-invasive

procedure, there appear to be a slower decline in weight of the patients with lower durability on the long term, on the other hand, LSG has longer sustaining effect on weight control despite being an invasive surgical procedure with longer hospital stay and higher incidence of side effects. [9, 10]

This lead to the question whether the cause of difference on durability of weight loss is related to a difference in hormonal change. This study aims at examining the effect of both procedures on the circulating leptin levels and its relation to the weight loss.

Materials and Methods

Two groups of totally 20 patients divided equally, underwent intervention for obesity treatment at Center Ain Shams Hospital and different private hospitals in Cairo between September 2014 and March 2015. Patients were selected by the gastroenterologist in cooperation with the nutrition team.

Group I: (control group) consisted of ten patients: Inclusion criteria were BMI>30 kg/m2 and need for preoperative weight loss. Patients with the following comorbidities at the time of balloon placement were excluded: acute gastritis, history of stomach surgery, Hiatus hernia, gastric and duodenal ulcers, hypertension (blood pressure >140/90 mmHg), fasting glycemia (>126 mg/dL), respiratory disorders (sleep apnea and/or tachypnea after little physical activity), pregnancy or coexisting severe hepatic, pulmonary, renal, cardiovascular, neurological, or psychiatric diseases.

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.

Group II: (case group) consisted of ten patients: The subjects had either body mass index (BMI) ≥ 40 kg/m2, BMI ≥ 35 kg/m2 with associated co-morbidities, or BMI < 35 kg/m2 with a history of weight loss resulting from intensive therapy followed by regaining weight. Patients with big hiatal hernias, gastroesophageal reflux disease, severe organ dysfunction, and major psychiatric dysfunction were excluded.

Collected blood by venipuncture was allowed to clot, and then separated serum by centrifugation at room temperature. Specimens were frozen at -20 °C till the time of the assay.

Leptin hormone level was measured before and 6 months after the procedures using DRG® Leptin (Sandwich) ELISA (EIA-2395). The DRG Leptin ELISA Kit is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle.

Results

The present study shows that the placement of Bioenteric Intragastric Balloon (BIB) for six months resulted in a statistically significant reduction in body weight. The mean loss of weight was 20 kg ranging from (15 kg to 28 kg), this demonstrates a beneficial effect of gastric balloon on body mass reduction in obese persons.

The mean weight loss was 30.4 kg with ranging from (20-39 kg) at six months after the laparoscopic sleeve gastrectomy and the mean preoperative weight was 128 kg with range(95-155kg), this demonstrates a beneficial effect of LSG on body weight reduction.

There was a statistically significant difference between the two groups (BIB and LSG) as regard the weight loss ($P<0.05$), which shows that there is a difference in the efficiency of weight loss between the two procedures.

Leptin showed a highly significant ($P<0.001$)decrease six months after the insertion of the balloon. The mean decline of leptin hormone level was 8 ug/l (+/- 5.06) as the mean preoperative level was 22.3 ug/l (+/- 5.96) and the mean postoperative level was 14.3 ug/l (+/- 3.77). This demonstrates the hormonal influence of BIB application, which is probably related to the decrease in the amount of adipose tissue, the source of leptin, after balloon application.

In the group of sleeve gastrectomy (SG), leptin showed a significant ($P <0.05$) decrease six months after the operation. The mean decline of leptin hormone level was 17.6 ug/l (+/- 17.06) as the mean preoperative level was 38.8 ug/l (+/- 24.83) and the mean postoperative level was 21.2 ug/l (+/- 8.68), this demonstrates the hormonal influence of LSG on the leptin hormone.

Table 1: Comparison between Sleeve gastrectomy group and Intra gastric balloon group as regard Weight loss

Groups	Weight loss						T-test	
	Range			Mean	±	SD	t	P-value
Sleeve gastrectomy	20	-	39	30.4	±	7.336	3.691	0.002*
Intra gastric balloon	15	-	28	20	±	5.055		

This table shows statistically significant difference between Sleeve gastrectomy group and Intra gastric balloon group as regard Weight loss when P-value was <0.05

Table 2: Comparison between Sleeve gastrectomy group and Intra gastric balloon group as regard Leptin preoperative

Groups	Leptin preoperative						T-test	
	Range			Mean	±	SD	t	P-value
Sleeve gastrectomy	17.0	-	100.0	38.80	±	24.83	2.093	0.068
Intra gastric balloon	12.0	-	32.0	22.30	±	5.96		

This table show statistically non-significant difference between Sleeve gastrectomy group and Intra gastric balloon group as regard Leptin preoperative when P-value was >0.05

Table 3: Comparison between Sleeve gastrectomy group and Intra gastric balloon group as regard Leptin Postoperative

Groups	Leptin Postoperative						T-test	
	Range			Mean	±	SD	t	P-value
Sleeve gastrectomy	14.0	-	43.0	21.20	±	8.68	2.306	0.033*
Intra gastric balloon	10.0	-	22.0	14.30	±	3.77		

This table show statistically significant difference between Sleeve gastrectomy group and Intra gastric balloon group as regard Leptin postoperative when P-value was <0.05*

Table 4: Comparison between Sleeve gastrectomy group and Intra gastric balloon group as regard Change in Leptin

Leptin	Regard Change						T-test	
	Range			Mean	±	SD	t	P-value
Sleeve gastrectomy	3.0	-	57.0	17.60	±	17.06	1.706	0.105
Intra gastric balloon	2.0	-	16.0	8.00	±	5.06		

This table show non statistically significant difference between Sleeve gastrectomy group and Intra gastric balloon group as regard change in Leptin when P-value was >0.05

Table 5: Correlation between Change in Leptin and Weight loss in both groups

Weight loss	Change in Leptin	
	r	P-value
Sleeve gastrectomy	0.585	0.076
Intra gastric balloon	0.809	0.005*

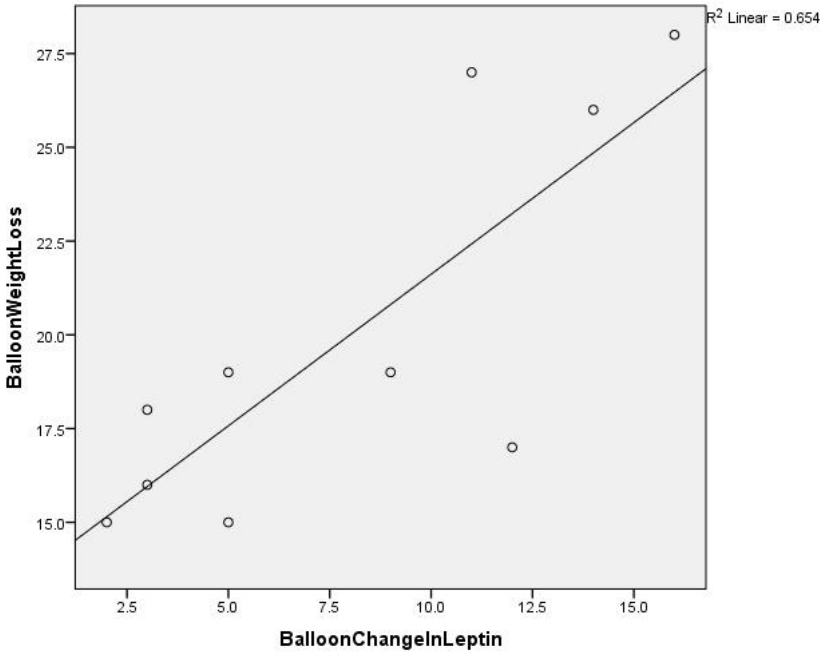

Figure 1: Positive correlation between Change in Leptin and Weight loss in group intragastric balloon when r=0.809 with p-value 0.005*

Discussion

As puzzling as it is, the level of decrease of leptin is more in the Gastric balloon group than the Sleeve Gastrectomy group, which indicates that the mechanism of hormonal intervention in the weight loss might be different, where the volume of the stomach is not the playing factor for the hormonal change but actually the volume of the effective mucosal cells present that play that role.

This was shown in a previous study where the repeated gastric distention in rats might have an effect on the neuroendocrine system, where it resulted in a decrease in the circulating leptin level, in spite of acquiring the same amount of caloric intake and having the same weight.[11]

The six months follow up duration is recommended in case of IGB but the regaining of weight is a common outcome on long term follow up of the patients [12].

In a study done by *Dastis et al.*, of the one hundred patients that started the study only 24 sustained their body weight loss after two and half years. [13]

On the other hand the weight loss is more determined with the actual size of the stomach and effective mucosal cells present, this may be due to not only hunger suppress by the central pathway through inhibition of the satiety center[14] but also due to the decrease in the acidity of the stomach by decreasing the volume of the HCL and pepsin secretion. This may result in a state of mild mal-absorption due to the lack of the preparation of the food in the stomach, leading to decrease absorption in the intestine, and hence decrease in the calorie benefit from the same meal the patient with bariatric surgery may take.[15]

That may lead us to think of different parameters when trying to measure the effectiveness of different bariatric procedures, for example lean more to the hormonal panel change in case of the decrease in the volume of the stomach, but more to just the BMI and weight loss in case of the surgical removal of an actual part of the stomach.[16]

Secondly, this may lead us to question the effectiveness of the different procedures on the long term, is the hormonal change more reliable for a keeping the lost weight on the long term or the mild malabsorption is the more effective due the continuous loss of the mucosal cells responsible for part of the digestion.[17]

Thirdly, whether it is really worth it; to remove a part of a functioning cell pool and change the process of digestion forever, with all the changes that takeplace in his body in terms of possible nutrient and vitamin malabsorption, with possible need for continuous vitamin supplementation to correct the defect.

Finally, it might be important to search for the change in the floral composition in the surgical removal in a part of the stomach (in this case the sleeve gastrectomy), where the decrease in the stomach acidity lead to change in the composition of the intestinal flora, with its effect on the energy balance state.

Conclusions

Neuroendocrine pathways play an important part in energy homeostasis, their effect on the control of obesity in various interventions procedures may give us more understanding of the process of which these treatment options causes weight loss, and this may give us the knowledge to select patients for various procedures and introduce the role of adjuvant hormonal therapy with these energy regulating hormones to control obesity.

Recommendations:

More research is needed for the complete understanding of the effect of different interventional procedures on the hormonal system and its relationship to the effectiveness of weight loss, in light of the arising recombinant hormonal therapy era, where it could open the door to hormonal adjuvant therapy to these procedures.

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