

SERUM LEPTIN LEVELS AND PANCREATIC ENDOCRINE FUNCTION IN BARIATRIC PATIENTS

Paula Dejeu¹, Viorel Dejeu^{2,3}, Dănuț Dejeu^{2,3}, Marius Bembea^{4,5}

¹Medical Laboratory, Bethany Medical Clinic Oradea, Bihor County, Romania

²General Surgery, "Dr. Gavril Curteanu" City Hospital, Oradea, Romania

³General Surgery, MedLife Genesys Hospital, Arad, Romania

⁴Pediatrics and Clinical Genetics, "Dr. Gavril Curteanu" City Hospital, Oradea, Romania

⁵Faculty of Medicine and Pharmacy, University of Oradea, Romania

ABSTRACT

Background. Leptin is a hormone synthesized and secreted by the adipose tissue, with a regulating role in the neuro-endocrine-metabolic functions in humans during fasting. Obesity associates metabolic syndrome which combines a leptin resistance status with an insulin resistance status, a disorder that increases the risk of occurrence of type 2 diabetes mellitus. After the bariatric treatment, the decrease of leptin levels in obese patients improves the endocrine function of the pancreas and decreases the risk of developing type 2 diabetes mellitus over time.

Aim. In the present study, we have monitored the dynamics of the serum values of leptin, insulin and glucose in correlation with the decrease of BMI (body mass index) after the bariatric surgery.

Material and methods. Glucose, insulin and leptin serum levels were assessed in 48 obese individuals before and at 6 months after the bariatric surgery.

Results. Leptin and insulin serum levels are decreasing significantly along with the decrease of BMI and pancreatic beta cells optimize their endocrine functionality.

Conclusion. Pancreatic endocrine function in obese individuals who undergo bariatric treatment improves significantly at 6 months after the surgery procedure.

Keywords: leptin, endocrine pancreas, insulin, obesity, bariatric surgery

BACKGROUND

Obesity is defined as a worldwide spread multifactorial polygenic disease, both in the developed countries, and in the emerging ones. The World Health Organization has defined obesity as a relapsing chronic disease [1]. The diagnosis and assessment of the obesity degrees is evaluated most frequently through the BMI (body mass index) which is calculated by the ratio between W and h² (kg/m²), where W represents the person's weight (kilograms), and h – height (meters). The treatment of obesity through surgical procedures bears the name of bariatric surgery and is taken into account in the case of obese individuals for whom the hygienic, dietetic and medicamentary therapy doesn't show any results. At the present day, bari-

atrics is the only treatment method that induces a significant and sustained weight loss in obese individuals, with a considerable improvement of the associated comorbidities [2-5]. As regards the secretory capacity of the adipose tissue, there have been demonstrated the complexity and metabolic activity of the adipocyte [6,7]. At present, the adipocyte is considered a glandular cell active from the endocrine point of view, with a complex secretory capacity that influences body weight control.

Leptin is a hormone secreted by the adipose tissue and is considered the "starvation signal". It decreases significantly during inanition periods determining the increase of glucocorticoids and the decrease of thyroxine, reproductive and growth hormones (STH, insulin) [8]. Moreover, the leptin decreases in thermogenesis during inanition and

the subsequent hyperphagia is being mediated, at least partially, by the decrease in the leptin's values [9]. Consequently, the leptin deficiency has been understood as a starvation status that induces compensatory responses such as hyperphagia, diminished metabolic rate and modifications in the hormone values for the purpose of restoring the energy values [9]. Chan and collab. [10] have studied the regulating role that the leptin has on the humans' neuro-endocrine-metabolic functions during fasting. The concepts of leptin resistance and insulin resistance have appeared upon the detection of certain high serum levels of leptin, glucose and insulin in obese individuals [11]. The insulin resistance represents a pathologic metabolic condition of the body in which a certain insulin concentration determines a suboptimal response at the level of peripheral tissues, thus the individual being predisposed to develop type 2 diabetes mellitus [12,13] over time. The effects of the insulin resistance emerge mainly at the level of tissues that depend on this pancreatic hormone as regards the intracellular transport of glucose in the liver, muscle and adipose tissues. On the other hand, the effects of insulin resistance are multiple due to the fact that the insulin plays a key-role in the glucidic, lipid and protein metabolism, as well as in the endothelial function [12]. The insulin resistance syndromes embody a clinically large range, among which we can include obesity, metabolic syndrome, glucose intolerance, diabetes mellitus and the extreme resistance status to insulin. The insulin sensitivity and its secretion at the pancreatic level are correlated; nevertheless, the insulin resistance presupposes a high insulin secretion in order to be able to maintain glycaemia and lipid homeostasis [13-16] within normal ranges. It is assumed that a certain number of mediators signalise the pancreatic beta cells in order to respond to the insulin's action. The absence of these signs or the incapacity of pancreatic beta cells to respond physiologically to the stimulus of these mediators induces an inadequate insulin secretion, modified glucose serum levels à jeun, low insulin tolerance and type 2 diabetes mellitus.

AIM

In the present study, we have monitored the dynamics of the serum values of leptin, insulin, glucose and the endocrin function of beta pancreatic cells in correlation with the decrease of BMI (body mass index) after the bariatric surgery.

MATERIAL AND METHOD

The present trial was conducted from January 2017 to September 2018 at the Medical Laboratory Department of Bethany Medical Clinic upon the patients who underwent bariatric treatment (gastric sleeve, gastric by-pass) at Med Life Genesys Hyperclinic Arad.

Study design and patients

The laboratory tests for the eligible patients were performed at Bethany Private Medical Clinic in Oradea. The subjects included in the study were obese individuals associating type 2 diabetes mellitus or a high risk of developing type 2 diabetes over time. The clinical evaluation included: weight, height, body mass index (BMI), abdominal circumference, blood pressure, family history of overweight/obesity and comorbidities. 635 patients were assessed before the bariatric surgery and 579 were eligible for the clinical trial. 109 patients were included in the study, from which 71 underwent a bariatric treatment and 48 were assessed both before and after the surgery procedure.

Statistical analysis

For the statistical analysis, a comparison of mean values was performed using the Student pair test for normal distribution variables and the Wilcoxon test for those with asymmetric distribution. The statistical significance limit was 0.05.

RESULTS

Incidence of type 2 diabetes in the preoperative studied group

The incidence of diabetes mellitus to the entire group of preoperative patients has been of 38.5% (42 out of the 109 enrolled subjects). But if we compare the group of patients that came to the postoperative assessment and the ones who didn't show up at the follow-up, we can observe a more reduced incidence of diabetes mellitus in the first group ($p = 0.0175$, Chi-square test with Yates' correction).

TABLE 1. Incidence of type 2 diabetes mellitus in the preoperative studied group

| Type 2 diabetes mellitus | Lost group (n = 61) | Studied group (n = 48) |
|----------------------------------|---------------------|------------------------|
| Present – number of patients (%) | 30 (49.2) | 12 (25) |
| Absent – number of patients (%) | 31 (50.8) | 36 (75) |

Type 2 diabetes evolution after bariatric surgery procedures

Comparing the incidence of type 2 diabetes mellitus pre- and postoperative it was recorded a statistically significant improvement.

Out of the 48 studied patients, 16 (33.3%) presented increased glucose serum values, *i.e.* pre-operative diabetes mellitus. At least 6 months after the surgery, only 3 (6.3%) still presented this diagnosis and other cases were not registered ($p = 0.0244$, chi-square test with Yates' correction).

TABLE 2. Statistical significance of type 2 diabetes mellitus evolution

| Type 2 diabetes mellitus | Preoperative (n = 48) | Postoperative (n = 48) | Statistical significance (p) |
|----------------------------------|-----------------------|------------------------|------------------------------|
| Present – number of patients (%) | 16 (33.3) | 3 (6.3) | p = 0.0244 |
| Absent – number of patients (%) | 32 (66.7) | 45 (93.7) | |

Correlations between BMI and insulin levels

This correlation is less tight, but crosses the statistical significance threshold. Case distribution is presented in figure 1.

Correlations between BMI and functional beta-pancreatic cells

It was recorded also a tight linear correlation between BMI and the improvement in functional beta-pancreatic cells (%B).

Correlations between glucose and leptin serum levels

The tightest positive correlation has shown the decrease of glucose serum levels with the decrease of the leptin serum level (figure 3).

DISCUSSIONS

The adipose tissue hormones – including leptin – have been correlated with the inducing of a deregulated metabolic status that favours, on the long term, the weight gain even if under intensive medicamentary treatment [17,18]. Our results concerning the endocrine role of the adipose tissue and the determination of leptin levels before and after bariatric surgery are similar with the results of other articles found in the specialized literature that demonstrate the efficiency of laparoscopic gastric resection in the reduction of obesity markers [19,20,21]. The improvement of insulin resistance in the postoperative patients has been previously proved, and is independent and more rapid than the weight loss [22]. The results concerning the insulin and glucose serum levels before meal – that were obtained in this study – are in accord with other similar studies [23,24] and point out a significant improvement in the insulin resistance and an improvement in the glucidic metabolism. In the case of patients with a short history of type 2 diabetes mellitus, the insulin resistance can be the major cause of diabetes, and not the dysfunctions

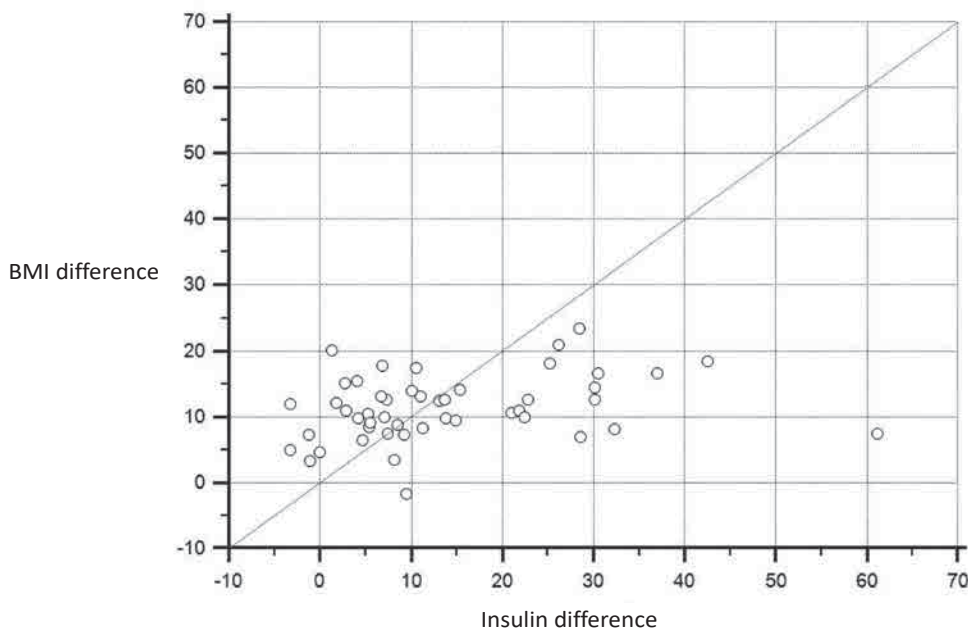


FIGURE 1. Case distribution based on decreasing BMI and postoperative insulin serum levels

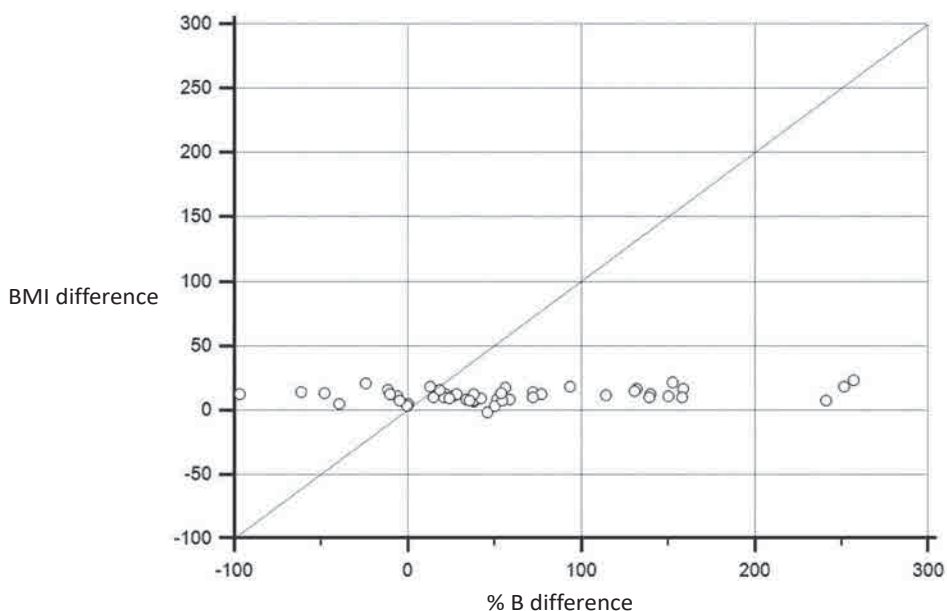


FIGURE 2. Case distribution based on BMI and functional beta-pancreatic cells

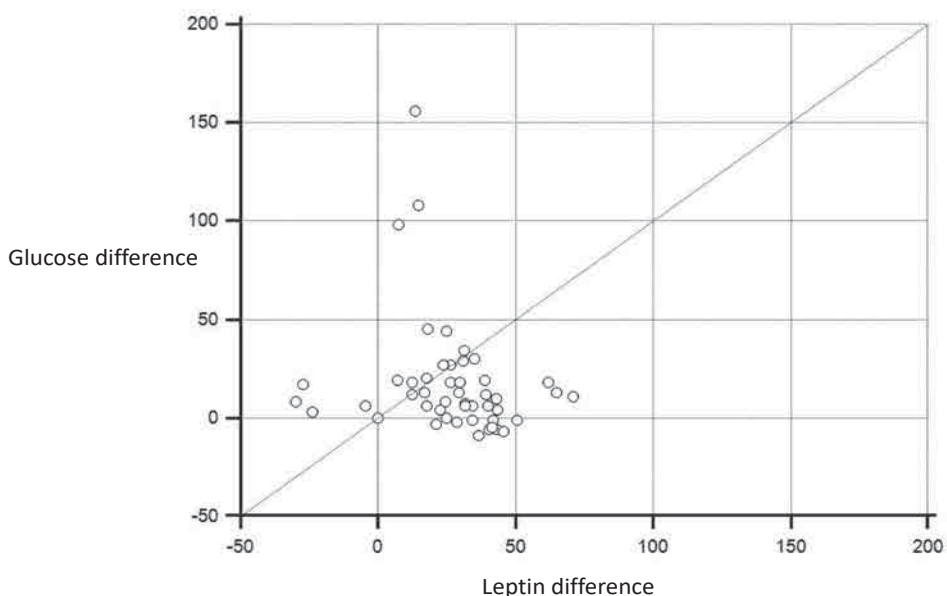


FIGURE 3. Case distribution based on postoperative decreasing glucose and leptin levels

of pancreatic beta cells [25,26]. Thus, the increase of insulin sensitivity is an efficient treatment for type 2 diabetes mellitus. The decrease in the percentage of functional pancreatic beta cells indicates an improvement in insulin resistance with a good long-term prognosis, the postoperative HOMA index being identified as an independent factor in predicting the complete remission response of diabetes [21,26,27]. Confirmation of the concept of altered carbohydrate metabolism by the release of adipokines from adipose tissue is also suggested by the analysis of correlations performed in the statistical study for this paper. Thus,

the linear correlation between the decrease in leptin serum levels and fasting glucose serum levels demonstrates this connection. The literature describes such linear positive correlations for different bariatric intervention methods (gastric by-pass [28] and gastric sleeve [29]) with similar results to this study.

CONCLUSIONS

As a synthesis and secretion hormone of adipocytes, the leptin alters the glucidic metabolism in obese individuals. Along with the decrease of

BMI, the glucose serum levels before meal register a decrease with a marked statistical significance after the bariatric treatment. The reduction of adi-

pose tissue optimizes the endocrine function of the pancreas by improving the secretory activity of pancreatic beta cells.

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