Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 3 Issue 9 September 2019

Conceptual

Thinking out of the Box during Management of Obesity

Giath Alshkaki Osman*

Infinity Surgical Associates, USA

***Corresponding Author:** Giath Alshkaki Osman, Infinity Surgical Associates, USA.

Received: August 20, 2019; **Published:** August 22, 2019

The rampant rise of obesity worldwide may soon be the most prevalent public health issue facing many nations including the US [Caballero, Moyer, Sturm]. Excessive body weight increases the risk for many diseases including diabetes, metabolic syndrome, cardiovascular diseases, and sleep apnea [Grundy]. Although obesity, defined as a body mass index (BMI) of 30 kg/m^2 or higher, is a preventable cause of death, its management has proven to be very difficult due to the compounded physical and mental comorbidities [Chiles, Peeters, Tsigosa]. Weight loss is the only predictable curative therapy. Many patients are able to lose some weight through specified diet plans, but maintaining the weight loss is very difficult to achieve, especially for those with significant obesity. Therefore, for patients with morbid obesity (BMI of 40 kg/m^2 or higher), the National Institutes of Health recommends bariatric surgery as the most effective treatment to reduce associated comorbidities [Robinson]. Bariatric surgery includes several surgical procedures all of which have a component of reducing the volume of the stomach. Most of these procedures result in weight loss, recovery from diabetes and obstructive sleep apnea, improvement in cardiovascular risks, and reduction in mortality [Adams, Vetter]. Among these procedures, sleeve gastrectomy performed laparoscopically is the one most preferred by patients.

The sleeve gastrectomy has proven as effective as other drastic surgical procedures for weight loss, but with the added benefit of reduced surgical risks and recovery complications. For instance, the chances for dumping syndrome, ulcers, intestinal obstruction, anemia, osteoporosis, protein deficiency, and vitamin deficiency are significantly reduced. With this procedure, most patients lose between 45% and 50% of their initial excessive body weight during the 6 to 12 months after surgery and maintain an optimum weight over the next five years. Maintaining the weight loss has been largely attributed to the removal of the fundus of the stomach that secretes the hormone ghrelin.

In obesity, feedback regulation of ghrelin seems to be modified by many epigenetic and environmental influences. In particular, DNA methylation, microRNA, mRNA, S-Adenosyl methionine (SAMe) plasma level, and inflammation processes caused by metabolic dysregulations may affect the expression of ghrelin and related hormones. DNA methylation is the addition of methyl group to DNA's cytosine base [Gallinari]. The methylated cytosine causes down-regulation of gene transcription. Similarly, histone acetylation of the lysine residues at the N-terminal removes the positive charge of histone reducing its affinity to DNA [Barnes]. Thus, histone acetylation enhances transcription and expression of genes. DNA methylation and histone acetylation modulate the condensation of chromatin and are directly related to the epigenetics of many diseases [Jaenisch]. DNA methylation is involved in nearly all neoplastic changes, and it is necessary for the epigenetic programming of genes involved in many diseases such as tumor progression. SAMe is a biological methyl donor and participates in many enzymatic reactions including DNA synthesis. Abnormal levels of SAMe or its cofactors affect DNA methylation and reduce the expression of ghrelin in animal models [Bossenmeyer-Pourie]. Leptin, an IL-6 analog, is a pro-inflammatory and contributes to the exacerbation of abnormal SAMe levels.

The inter-dependency between ghrelin, leptin, obestatin, insulin, glucagon, and thyroid hormones are still the subject of exten-

sive research [Ren, Egido]. Patients undergoing laparoscopic sleeve gastrectomy (LSG), where the greater curvature of the fundus is resected, have a significant decrease of plasma ghrelin immediately following surgery which continues to remain low and stable up to six months postoperatively [Langer, Hoda]. Presumably the level of obestatin is also drastically reduced. The level of leptin may also be reduced as P/D1 cells of the stomach also release leptin, although not significantly. It is believed that the effects of sleeve gastrectomy are due to the upregulation of ghrelin receptors in the brain and the physical limitation of the small remaining stomach, which inhibits excessive food intake. Despite the success of sleeve gastrectomy, there is a small number of patients who do not seem to fully benefit from the procedure. The purpose of this study is to investigate mechanisms contributing to this variable response. We seek genetic and epigenetic markers that correlate with the basal metabolic rate (BMR), ghrelin, leptin, and related hormones to identify subjects with obesity who can benefit from surgical interventions versus those who can be managed by dietary and pharmaceutical interventions. Thus we seek to establish new guidelines for the treatment of obesity and its co- morbidities, predict the outcomes of such treatments, and establish guidelines for early pharmacological interventions to prevent weight gain in successfully treated morbidly obese patients.

I suggest that future studies should satisfy the following Objectives to uncover the secrets of obesity and metabolism.

Investigate the inter-dependency between ghrelin, leptin, obestatin, insulin, glucagon, and thyroid and parathyroid hormones and identify the mechanisms regulating maintenance of weight loss following laparoscopic sleeve gastrectomy (LSG).

Identify genetic and epigenetic markers that correlate with BMR, ghrelin, leptin, and related hormones to identify subjects with obesity who can benefit from surgical interventions versus those who can be managed by dietary and pharmaceutical interventions.

Identify the associations between ghrelin, leptin, and obestatin plasma levels and the endocrine and hormonal mechanisms that lead certain patients to gain excessive weight after LSG and determine whether pharmacological interventions are necessary.

Develop a computer model to provide a better understanding of obesity and patient response to treatment, and to establish guidelines for early pharmacological interventions to prevent weight regain in successfully treated morbidly obese patients.

Volume 3 Issue 9 September 2019