Gastrointest Interv 2014; 3:80–83

Contents lists available at ScienceDirect

Gastrointestinal Intervention

journal homepage: www.gi-intervention.org

Review Article

Bariatric embolization for the treatment of obesity

Charles Y. Kim,[1,*] Ben E. Paxton,[2] Clifford R. Weiss,[3] Aravind Arepally[4]

A B S T R A C T

Embolization of the left gastric artery with the intent of decreasing hunger, termed bariatric embolization, has experienced a recent surge of attention in the literature and at medical conferences. This endovascular treatment for obesity has demonstrated promising data as a potentially new and effective minimally invasive treatment for obesity. The goal of this review article is to discuss the background, rationale, and existing data on this new topic.

Keywords: Bariatric, Embolization, Obesity

Introduction

Bariatric embolization, also known as left gastric artery embolization, is a recently introduced endovascular image-guided procedure aimed at treating obesity.[1] This procedure entails percutaneous transarterial particle embolization of the gastric fundus arterial supply, which is the site of the highest concentration of ghrelin-secreting cells in the body. By doing so, it is hypothesized that the intentionally induced ischemia in the gastric fundus will result in depressed serum ghrelin levels, which may decrease hunger, decrease food intake, and thereby induce weight loss. The goal of this review article is to discuss the background, rationale, and existing data on this new and burgeoning topic.

Obesity

In 1997, the World Health Organization designated obesity as a global epidemic, marking the first time in history that a noninfectious malady has been labeled as an epidemic.[2] In 2008, >1.4 billion adults were overweight, with a body mass index (BMI) of ≥25. Five hundred million were obese, with a BMI of ≥ 30.[3] Thus, 11% of the world's population was classified as obese. The rate of obesity is growing, with an incidence that has nearly doubled since 1980.

Obesity is ranked as the fifth leading risk for mortality globally.[3] Obesity has been strongly linked to numerous comorbidities, including type II diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, cancer, and depression.[4] The link is actually strong – for example, the risk of diabetes increases 18-fold in obese patients. The increase in relative risk of coronary artery disease in middle-aged men is 72% higher, even with only mild obesity. In aggregate, these obesity-related comorbidities have been reported to be responsible for >2.5 million deaths per year worldwide. Not surprisingly, life expectancy is profoundly affected by obesity. For example, a 25-year-old morbidly obese man can expect a 22% reduction in lifespan.[5] In fact, an expert panel convened by the National Institutes for Health stated that for the first time in history, the steadily improving worldwide life expectancy could level off or even decline within the first half of this century, specifically as the result of the increasing prevalence of obesity.[6]

The fundamental cause of obesity is an energy imbalance, with more calories being consumed than expended. The global rise in obesity can be attributed at least in part to the increased intake of high-calorie and high-fat foods and a decrease in physical activity related to the increasingly sedentary lifestyles resulting from modernization and automation. However, numerous additional etiologies and pathologies are also known to be responsible for obesity.

Regulation of hunger

The hormonal regulation of hunger is complex, and is primarily governed by hunger-inhibiting hormones.[7] Mechanical and chemical factors associated with meals stimulate enteroendocrine cells, resulting in signals transmitted neutrally through vagal nerves and/or circulating hormones. The end result is modulation of hunger in the central nervous system. Short-term hunger modulation in response to meals is largely due to cholecystokinin. Longer-term regulation of energy balance and weight is controlled largely by the effects of insulin and leptin. Although >40 hormones

[1] Division of Vascular and Interventional Radiology, Duke University Medical Center, Durham, NC, USA
[2] Vascular and Interventional Specialists of Prescott, Prescott, AZ, USA
[3] Interventional Radiology Center, Johns Hopkins Hospital, Baltimore, MD, USA
[4] Division of Interventional Radiology, Piedmont Radiology, Atlanta, GA, USA
Received 13 September 2014; Revised 7 October 2014; Accepted 8 October 2014
* Corresponding author. Division of Vascular and Interventional Radiology, Department of Radiology, Duke University Medical Center, Box 3808, Durham, NC 27710, USA.
E-mail address: charles.kim@duke.edu (C.Y. Kim).

2213-1795/$ – see front matter
http://dx.doi.org/10.1016/j.gii.2014.10.004

have been shown to inhibit appetite, only ghrelin has been shown to stimulate appetite.[7]

Ghrelin

Ghrelin is a peptide hormone that is secreted primarily from the gastrointestinal tract, with the highest concentration in the fundus of the stomach, with progressively decreasing concentrations in the small and large intestines. Ghrelin was first identified and reported in the literature in 1999 as an endogenous ligand for the growth hormone secretagogue receptor.[8] Additionally, ghrelin directly stimulates appetite and induces positive energy balance, resulting in body weight gain. Ghrelin is also expressed in the pancreatic islets, hypothalamus, and pituitary gland. In addition to stimulating appetite, ghrelin has also been shown to increase circulating growth hormone, adrenocorticotropic hormone, cortisol, prolactin, and glucose.[9] Given the relatively recent discovery of ghrelin and incomplete understanding of its functional role, it likely has additional effects on other hormones and functions. Due to the unique nature of this hormone and its effect on appetite, multiple approaches to modulate ghrelin production have been attempted. Although various reports of ghrelin suppression have been described, none to date have been clinically practical, including intraventricular and large intraperitoneal delivery of ghrelin antagonists in rats, as well as a ghrelin vaccine.[10–13]

Gastric distribution

The detailed distribution of ghrelin-expressing cells has been reported in two separate studies.[14,15] Although Kim et al[14] analyzed gastric specimens from patients with gastric cancer undergoing total gastrectomy, Goitein et al[15] analyzed resected gastric specimens from patients undergoing sleeve gastrectomy, which entails vertical resection of most of the stomach volume, including the entire fundus, most of the gastric body, and part of the antrum. In both studies, polymerase chain reaction analysis of ghrelin mRNA and immunostaining for ghrelin-expressing cells were performed throughout the resected specimen. In both studies, ghrelin mRNA and ghrelin-expressing cells were identified throughout the entire stomach; however, the concentrations of ghrelin mRNA and ghrelin-expressing cells were statistically highest in the gastric fundus, and lowest in the gastric antrum. Kim et al[14] reported a ghrelin/actin mRNA ratio of 0.78 in the fundus, 0.20 in the body, and 0.07 in the antrum, reflecting a 10-times higher ghrelin concentration level in the fundus compared to the antrum. Goitein et al[15] similarly reported a ghrelin/ribosomal mRNA ratio of 0.043, 0.026 and 0.015, respectively, which is an approximately three-times higher level in the fundus than antrum.

Treatment options for obesity

Diet and exercise regimens, while effective, have been shown to be difficult to maintain in the long term.[16] Plasma ghrelin levels have been shown to rise sharply shortly prior to meals, which correlates with hunger that occurs just prior to consuming meals.[17] Conversely, ghrelin levels fall shortly after each meal, which correlates to the satiation of hunger after consuming food. Diet regimens to induce weight loss have been shown to be difficult to sustain, due to the increase in hunger.[16] Thus, it may not be surprising that dieting induces a 24% increase in the 24-hour ghrelin profile ($P = 0.006$).[17] This elevated ghrelin secretion may therefore be a reason why dieting is so difficult to sustain in the long term.

Pharmacological modulation of hunger would be perhaps the ultimate means of controlling appetite and weight. Despite great efforts in this area, current pharmacotherapeutics can achieve only modest levels of weight loss with a range of 2.0–6.5 kg of sustained weight loss.[17]

Although bariatric surgery has proven to result in substantial degrees of sustained weight loss, the surgical risk in this patient population is significant. Alterations in ghrelin levels also occur with bariatric surgery. After gastric banding, there has been shown to be a 27% increase in serum ghrelin levels, which may be undesirable if patients experience increased hunger.[18] The results with roux-en-Y gastric bypass are somewhat controversial. Although some studies have demonstrated a decrease in serum ghrelin, others have shown ghrelin levels to be unchanged.[19–21] However, with sleeve gastrectomy, the levels of serum ghrelin have been shown in multiple studies to be markedly decreased by ~60%.[20,21] In fact, ghrelin depression has been shown to be significantly depressed even as far as 5 years post-surgery.[22] Considering that the majority of the gastric fundus is removed during sleeve gastrectomy, there would certainly be a loss of a large proportion of ghrelin-secreting cells. Many have postulated this as one of the primary reasons why sleeve gastrectomy is the most effective of the bariatric surgeries, and conversely, a reason why surgeries that have no gastric tissue resection, such as gastric banding, have poor efficacy.

Gastric artery chemical embolization

The initial discovery that introduced the concept of destruction of ghrelin-producing cells by minimally invasive catheter-directed techniques was reported by Arepally et al[23] in 2007. In this pilot study, the authors demonstrated that infusion of sodium morrhuate, a varicose vein sclerosant, into the left gastric artery of swine resulted in elevated serum ghrelin levels with low doses, but depressed serum ghrelin levels at moderate doses. Notably, at high doses, death resulted secondary to gastric necrosis and perforation. Arepally went on to perform gastric artery chemical embolization (GACE) in a larger number of swine using the higher doses, with a control arm to assess for differences in ghrelin level and weight over a 4-week period.[24] Again, the serum ghrelin levels in treated animals were shown to be significantly depressed compared to controls. In these growing swine, the mean weight was statistically lower at 3 weeks and 4 weeks compared to untreated controls. However, the mean serum ghrelin levels demonstrated a 51% increase at 4 weeks, suggesting that the effect may be transient.

Bariatric embolization in a porcine model

The use of sodium morrhuate, while promising in the initial studies, would be difficult to translate to use in humans. This long-used sclerotherapy agent is used to induce direct damage to the endothelium of varicose veins. As a liquid agent, control of the distribution of flow can be difficult to control. The appropriate amount to administer would also be difficult to ascertain given variability in stomach size and vascularity. A well-described complication of sodium morrhuate use in venous sclerotherapy is inadvertent flow to the lungs, which causes pulmonary arterial injury and even respiratory failure.[25] Even more worrisome is its ability to induce transmural necrosis and perforation when infused into the gastric arteries.[23]

Rationale

In an effort to destroy ghrelin-secreting cells in the gastric fundus using an agent that is benign, more controllable, and potentially easily translatable to human trials, our research group investigated the effect of ischemia by means of particle embolization of the gastric fundus as a method to potentially impair the