Sleeve gastrectomy as evolution in management of morbid obesity

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استئصال المعدة العمودى كتطور فى علاج السمنة المرضية

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Abstract

The rising prevalence of morbid obesity and the increased incidence of super-obese patients (BMI >50 kg/m^2) seeking surgical treatments has led to the search for surgical techniques that provide adequate excess weight loss (EWL) with the least possible morbidity. Sleeve gastrectomy (SG) was initially added as a modification to the biliopancreatic diversion (BPD) and then combined with a duodenal switch (DS) in 1988. It was first performed laparoscopically in 1999 as part of a DS and subsequently done alone as a staged procedure in 2000. With the revelation that patients experienced weight loss after SG, interest in using this procedure as a bridge to more definitive surgical treatment has risen. Benefits of SG include the low rate of complications, the avoidance of foreign material, the maintenance of normal gastro-intestinal continuity, the absence of malabsorption and the ability to convert to multiple other operations. Reduction of the ghrelin producing stomach mass may account for its superiority to other gastric restrictive procedures. SG should be in the armamentarium of all bariatric surgeons. Nonetheless, long-term studies are necessary to see if it is a durable procedure in the treatment of morbid obesity.

Key words:

Bariatric surgery; Laparoscopy; Morbid Obesity; Sleeve gastrectomy; Weight loss

Contents

Introduction

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Aim of the work:

The aim of this study was to evaluate the efficacy of Laparoscopic Sleeve Gastrectomy (LSG) as a definitive procedure for morbidly obese patients considering the complications and the long-term effect on weight loss.

Definition of obesity:

Obesity is likely to be the disease of the 21st century. The grow of obesity is worldwide, a pandemic, with the World Health Organization estimating more than 1.6 billion people are currently overweight and 400 million obese **(WHO, 2000)**. Obesity is characterized by an excess of adipose tissue. The most commonly used measurement for determining obesity is the body mass index (BMI), which is calculated as the weight (kg)/height (m^2) **(NIH, 2003)**. Although there are some limitations for measuring obesity by the BMI, but it is an index that provides a measurable estimate of body fat and it is related to the risk of complications associated with obesity **(Kushner and Roth, 2003).**

The National Institute of Health (NIH) published an important document in 1998 entitled Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. This approach is also compatible with that adopted by the World Health Organization (WHO).

The normal range for the BMI is 18.5 – 24.9 (kg/m^2),

Overweight(grade 1 overweight) the BMI is 25.0 – 29.9 (kg/m^2),

Obesity (grade 2 overweight) the BMI is 30.0 – 39.9 (kg/m^2),

Morbid obesity (grade 3 overweight) the BMI is over 40.0 (kg/m^2).

These categories correspond to popular descriptions of normal weight, overweight, obesity and morbid or extreme obesity. Recent studies showed that aside from fat tissue function as excess energy storage, but also as endocrine organ which produces various substances that affect body metabolism **(Considine, 2002).** Etiology of obesity is often difficult to be determined. It is important to understand the pathogenesis of obesity specially energy regulation mechanism in order to provide appropriate management of obesity **(Rosenbaum et al., 1997).**

Pathogenesis of obesity:

The definite etiologic cause of obesity remains unclear. There are 3 main factors (genetic, environment, energy balance) involved in the pathogenesis of obesity which are related to one another in a complex interaction.

- **Genetic factor:**

It is estimated about 30% and 50% of body weight gain is due to genetic factor. Study on families of obese patients had proven the existence of significant relationship of BMI between members of family among one generation. Until recently, we have identified 7 genetic disorders which cause obesity in human. They are gene signals of leptin, leptin receptor, melanocortin receptor 4 (MC4), alpha-melanocyte stimulating hormone (a-MSH), prohormone convertase 1 (PC-1), proopiomelanocortin receptor (POMC), peroxisome proliferators activated receptor gamma (PPAR-g) gen **(Seng, 2004).**

These genetic disorders consist of monogenic and multigenic disorder :

i. Monogenic disorder:

In obesity due to single gene disorder, Body Mass Index (BMI) may reach as high as > 60 kg/m^2, and has occurred since childhood. For example Prader-Willi syndrome which is caused by disappearance of material expression of paternal active genome in chromosome 15q11-13. The manifestation of the syndrome is short gesture, fat deposition in upper body, mental retardation, and hypogonadism. This disorder is very rarely found **(Rosenbaum et al., 1997).**

ii. Multigenic disorder:

Obesity phenotype is presumed as the result of simultaneous interaction of genetic disorders and environment factor. Various genes that have been mentioned above are responsible for fat distribution, energy expenditure during activity and rest, eating habit, lipase protein activity, basal metabolic rate, insulin induced-fat synthesis and decreased effect of thermogenic factor of the food

- **Environment factor:**

Environment factors that contribute to obesity are factors that cause increased food intake and decreased physical activity. Some factors suggested to promote overeating like portion size, high glycemic index of foods, accessibility of food, soft drinks, low cost of food, sugar, taste of food, fast foods, variety of food and low calcium & others that suggested to reduce physical activity like reduced need for physical labor in most jobs**,** no required physical activity in schools and reductions in physical activity required for daily living **(Hill and Donahoo, 2002).**

▪ Energy balance factor:

Energy balance consists of intake regulation and energy expenditure of the body. These are influenced by Psychological and Organobiological aspect.

Psychological aspect:

Perception of hunger is many times determined by mood, place, taste, type of food, eating behavior in family, local culture and eating motivation. Energy expenditure is much influenced by decreased motivation to exercise due to facilities and technology and lack of understanding on the benefit of physical activity for health maintenance **(Kurniasih and Indriyanti, 2001).**

Organobiological (Homeostatic) aspect:

Physiologically, energy intake is derived from food. The energy is produced to maintained basal metabolic rate (obligatory energy expenditure), adaptive thermogenesis energy and energy for working**.** If there were increased intake or decreased energy expenditure, the body would try to reduce excess energy and lower intake or increase energy expenditure. The extra energy in the long term will be stored in form of fat mass in adipose tissue. Protein and carbohydrate storage is relatively stable, thus, condition that determines the body weight in the long term is adipose tissue mass **(Jequier and Tappy, 1999).**

- Energy (food) intake regulation:

Physiologically, food intake is controlled by appetite which is the result of stimulus interaction of food and its inhibitors. Food stimulation is caused by

increased need and expenditure of energy in the form of hunger sensation, while the inhibitory factor is in the form of satiety. Hunger is influenced by internal factors such as blood glucose, insulin, ghrelin and external factors like emotion, time, food availability and environment factors. The sense of satiety has more roles in determining food quantity and much more influenced by internal factors **(Jequier and Tappy, 1999).**

There is feedback mechanism of food intake regulation consists of:

• Center of intake regulation and energy expenditure:

Hypothalamus is the center of information that receives and processes regarding energy balance status in the body through afferent signal derived from gastrointestinal tract and adipose tissue. Ventromedial hypothalamic nuclei (VHN) stimulation causes the release of neuropeptide of 'satiety' sensation. On the other hand, stimulation of lateral, dorsomedial and paraventriculi hypothalamic nuclei cause the release of neuropetides of 'hunger'. At the hindbrain, there are solitary tract nuclei (STN) which receive signal from gastrointestinal tract. Third brain ventriculi had arcuata nuclei which function as peripheral signal transducer to special neuronal signal. Those various nuclei are connected to one another and send signals through neurons to cerebral cortex, hypofisis brain stem cell and autonomic nerve system.

• Afferent Signal of Intake Regulation There are two afferent signals which are classified as hormonal and neuronal signal:

Hormonal signal:

This afferent signal comes from adipose tissue, gastrointestinal tract, thyroid glands, adrenal, muscles and reproductive organs where signals from the first two mentioned organs have more roles. These signals deliver information on

nutritional balance and body fat mass. Functionally, hormonal signal consists of short - term signal coding of satiety, while the long-term signal code energy balance in adipose tissue (adipocyte signal) **(Tschop and Horvath, 2003).**

Peripheral afferent signal of gastrointestinal tract during eating and digestion process, cholecystokinin (CCK) is released due to mechanical stimulation of gastric stretching. This hormone delivers afferent signal through vagal nerve to solitary tract nuclei (STN) which then projects it to hypothalamus, insular cortex and motoric nuclei of brain stem cell resulting in signal of cessation of eating processes **(Druce et al., 2004).**

Peripheral afferent signal of pancreas Insulin, glucagons, and amylin are food intake regulator. Adipocyte signal in condition of excess energy exists, secretion of insulin and leptin will increase as adipose signal that gives information to hypothalamus. On the contrary, in condition of insufficient energy, there is increase of ghrelin. Adipose signal is a long term signal although ghrelin and insulin are rather short-term signals **(Benoit et al., 2004).**

Main adipose signals are:

Leptin:

This substance is assumed as one of cytokine family due to its crystal structural form. Leptin is mainly produced in the night by white adipose tissue although it is also produced by the brown adipose tissue, gastric mucosa, macrophage, mammary epithelium, myocites, and placenta as well. Leptin level is in accordance with visceral adipose tissue, circulates freely or protein binds and is able to run across the blood brain barrier. In condition of long fasting, leptin level will decrease and the other way goes in excess food intake. Leptin

possesses receptors in hypothalamic tissue, brain, lung, renal, muscle, liver, pancreatic b - cell, adrenal, hemopoetic stem cell, ovary, and adipose tissue. Leptin secretion is increased by high dose insulin, glucocorticoids, and estrogen, while isopreterenol, adrenal b3 receptor agonist, nicotine, high Zn diet, thiazolidinediones, testosterone, and thyroxine will decrease it. Because leptin secretion is in line with the amount of fat mass tissue, thus obese patients have high level of leptin. This fact has explained the role of leptin resistance in the pathogenesis of obesity **(Sahu, 2004).**

Leptin binds with LEP-Rb in arcuate nuclei, leptin inform the condition of excess energy to hypothalamus through sympathetic nerve system. Leptin increases sympathetic activity which modulates thermogenesis through mitochondrial uncoupling protein (UCP) induction of brown adipose tissue .In addition, it inhibits lipogenesis and increases mitochondrial oxidation and lipolysis and makes intracellular fatty acid and triglyceride decrease **(Flier, 1998).**

Ghrelin:

Active form of ghrelin called n-octanoyl ghrelin is a potential oxygenic substance. This hormone which is found in gastric lamina propria capillary, intestine, kidney, placenta, hypofisis, and hypothalamus happen to be endogenic ligand of growth hormone secretagoge receptor (GHSR). It regulates appetite independently from its effects on growth hormone secretion. Ghrelin increases the expression of agouti related protein (AGRP) mRNA and neuropeptide Y (NPY) on hypothalamic arcuate neurons and inhibits vagal nerve activity. Strong stimulation of ghrelin secretion is low blood glucose level as signal to start eating. In weight loss condition, synthesis of ghrelin is increased to stimulate appetite. In obesity, plasma level of ghrelin is decreased and so that

obese patient will not gain extra energy. Ghrelin increases adipose mass because it reduces fatty acid oxidation. There has not been any report on the presence of ghrelin resistance. By its effect on appetite and fat mass, ghrelin has a role to regulate balance of energy both in short-term and long term of action **(Druce et al., 2004).**

Ghrelin is secreted by the endocrine cells of the stomach (X/A-like cells), which reside in the oxyntic glands of the gastric fundus. Gastric ghrelin producing cells are in contact with the basolateral membrane adjacent to the blood-stream and most of them do not come in contact with gastric content **(Neary et al., 2004)**.

Insulin:

This hormone functions to facilitate glucose influx into the cell and is necessary for fat synthesis and storage. Insulin level and secretion correlated positively with bodyweight and body fat content, especially white fat. Obese patients have fat more than normal people so that they will have basal and post prandial insulin higher and finally cause insulin resistance. Hyperinsulinemia in this condition increases fat absorption in adipose tissue **(Benoit et al., 2004).**

It is clear that insulin has the catabolic effect on central nervous system. When the level of insulin goes high, insulin influx rate into the brain is not increased. Insulin also has a role in long term signal processing through its ability to determine how much fat is needed and stored in the body. Insulin effect in peripheral and central nervous system seems to counteracts to each Other **(Inui, 2000).**

Neuronal Signal System:

The system is controlled by sympathetic and serotonergic nervous system which possesses axis that is very similar to adiposity signal axis. The role of sympathetic nerve system in regulating of energy intake is done by 2 actions. First by increasing thermogenesis through norepinephrine release which causes stimulation of mitochondrial UCP system. The second one is through increasing epinephrine release that will induce glucose and fatty acid oxidation. Serotonin neurons in dorsal raphe nucleus midbrain sends signals resulting in decreased food intake. Sympathetic neuronal signal system is also influenced by corticosteroids, estrogen, testosterone, and thyroxine **(Tschop and Horvath, 2003).**

- Energy expenditure regulation:

Nutrients derived from food digestions will undergo oxidative phosphorilation in mitochondria to form adenosine-triphosphate (ATP) by releasing energy in form of heat. The use of ATP and physical activity also releases heat. This process is initiated by sympathetic stimulation on b3-adrenergic receptor. The receptor stimulation will activate protein kinase A effectors and cyclic adenosine monophosphate (c-AMP) that has 2 effects. The first is an acute effect of increased lipolysis and activation of UCP-1 on brown fat tissue and UCP-2 and UCP-3 of muscles. The second is a chronic effect such as UCP gene transcription, mitochondrial biogenesis, hyperplasia, and brown adipose tissue recruitment to white adipose tissue. Propiomelanocortin (POMC) system regulates energy expenditure through melanocyte stimulating hormone (□-MSH) neurons on melanocortine receptor 4 (MC-4) by activating sympathetic nervous system. Activation of POMC neurons is initiated by leptin when energy storage in fat tissue is increased **(Lowell, 2002).**