Introduction

Obesity is a state of excessive storage of body fat. The prevalence of obesity has been progressively increasing worldwide, and is closely associated with increased morbidity and mortality. The co-morbidities include many pathological conditions; the most common and important are diabetes, hypertension, cardiovascular diseases, and cancer (Gidding et al, 1996, Allison et al., 1999, Faloia et al., 2000).

The World Health Organization (WHO) estimates that over a billion adults are overweight and over 300 million are obese worldwide. The annual cost of managing obesity in the United States alone amounts to approximately 100 billion dollar, of which approximately 52 billion dollar are direct costs of healthcare. These costs amount to approximately 5.7% of all US health expenditure. The cost of lost productivity due to obesity is approximately 3.9 billion dollar, and another 33 billion dollar is spent annually on weight-loss products and services (Pieter et al., 2008).

Apart from total body fat mass; accumulating data suggest that regional fat distribution substantially affects the incidence of co-morbidities associated with obesity. High abdominal and subcutaneous fat content is strongly correlated with worsened metabolic and clinical consequences of obesity (Allison et al., 1999). Obesity is associated with a potential co-morbidity that significantly increases the potential morbidity and mortality associated with the condition. Although no cause-and-effect relationship is exhaustively demonstrated for all these co-morbidities, amelioration of these conditions after substantial weight loss suggests that obesity probably plays an important role in their development (Allison et al., 1999, Friedman, 2000).

Obesity is a multifactorial process with complex interactions among genetic, metabolic, hormonal and psychological factors. It may never be possible to point to a single factor as being the predominant cause of obesity.

In recent years, we have begun to realize that adipose tissue is more than just a passive depot for excess energy (Ahima and Flier,

2000). Indeed, as several studies have shown, adipose tissue is a metabolically active tissue that expresses and secretes a large number of proteins. Such molecules, called adipocytokines, have a hormone- like action and interfere with basal and glucose metabolism [Bouret and Simerly, 2004; Busetto et al., 2004).

Various studies have shown that adipose tissue is metabolically active, and secretes a large number of protein molecules which have hormone-like action and interfere with basal and glucose metabolism. Some of these hormone-like substances produced by adipose tissue are leptin, adiponectin, resistin and TNF-α.

Leptin, resistin, tumor necrosis factor-a (TNF-a) are increased in obese patients as a result of increased production by enlarged fat cells. In contrast, adiponectin, which improves glucose handling by peripheral tissues, is present at lower levels in obese patients (Bastard et al., 2002; Borst, 2004).

Leptin, produced in increased quantities by hypertrophic fat cell, could have a central role in the metabolic changes recorded after

liposuction. Indeed, the hormone leptin is the central mediator in a negative feedback loop regulating energy homeostasis (Ahima et al., 1996). Leptin administration leads to reduced food intake, increased energy expenditure, and weight loss (Halaas et al., 1995; Pelleymounter., 1995). Leptin also mediates unique metabolic effects, specifically depleting lipid from the peripheral tissues (Farooqi et al., 2001).

Increased body fat content is accompanied by low insulin sensitivity, which is compensated by increased insulin secretion (Larsson et al., 1996). Carantoni et al., 1998 found that the higher the fasting plasma leptin concentration, the greater the degree of insulin resistance. Their findings indicated that leptin acts through the functional leptin receptor in pancreatic islets to inhibit insulin secretion and provides evidence that hyperleptinemia might be a part of a link between obesity and diabetes.

The major role of leptin in body-weight regulation is to signal satiety to the hypothalamus and, thus, reduce dietary intake and fat storage while modulating energy expenditure and carbohydrate metabolism to

prevent further weight gain (Ahima and Flier, 2000). Ob/Ob mice were the prototype mice that enabled the discovery of leptin. These mice lack the leptin gene and are overweight and hyperphagic. A few humans with a similar genetic defect and similar phenotypic consequences have been identified. This variant of obesity, though minor in the grand scheme of human obesity, is exquisitely sensitive to leptin injection, with reduced dietary intake and profound weight loss. Unlike the Ob/Ob mouse model in which this peptide was first characterized, most humans who are obese; are not leptin deficient but rather leptin resistant. Therefore, they have elevated circulating levels of leptin (Chicurel, 2000). In 1995 several groups showed that leptin injections were capable not only of inducing dramatic weight reductions in very fat *ob* mice but were also able to reduce overfed normal mice (Larsson et al, 1996, Kronfeld-Schor et al, 2000, Harris, 2001).

Hypertrophic fat cells present in the subcutaneous tissue of obese patients generally produce increased quantities of secreted products such as leptin (Friedman, 2000).

Suction assisted lipectomy is the most common aesthetic procedure done worldwide (Shelton and Rokhsar, 2008). However, liposuction was intended for the body contouring rather than weight reduction. Most obese patients are overweight and they are usually concerned by weight reduction as well as restoration of body contouring. Recently, and with the advances in the anesthesia, plastic surgeons could perform liposuction of major amount of fat to serve both indications.

Recent study investigated the effect of liposuction on blood leptin levels. It was found that in most patients the level of blood serum leptin correlated with the body mass and fatty tissue index. A removal of limited volumes of fatty tissue results in an elevated level of blood serum leptin. The aspiration of greater volume of fatty tissue is followed by the primary decrease of the leptin level which further reaches to the initial level (Shcheglova et al, 2004).

Morbidly obese patients who underwent gastroplasty and diversion and developed massive weight loss, recorded considerable decrease in serum leptin which persisted at low

level long time postoperative (Admai et al, 1998). Another study reported a decrease in plasma leptin level in four patients underwent liposuction (Chen et al, 2001). The decrease in leptin was correlated with the volume of removed fat

Zicardi et al., (2002) studied the effect of large volume liposuction on the inflammatory cytokines and improvement of endothelial functions in obese women after weight loss over one year. They found significant and constant decline in TNF-α and IL-6 levels. So, weight loss represents a safe method for down regulating the inflammatory state and ameliorating endothelial dysfunction in obese women (Grzegorz et al., 2004).

Large volume liposuction is associated with continuous weight loss, improvement of glucose handling and lower inflammatory markers. The fat mass removal is significantly correlated with decrease in plasma triglycerides, free fatty acids, insulin, and leptin levels. With regard to inflammatory markers the amount of fat removal is correlated with decreasing plasma interleukins and TNF- α

levels. After 40 days there is a significant decline in these parameters (Rizzo et al., 2005).

Pamieri et al., (1995) utilized ultrasound and suction assisted lipectomy in 205 obese subjects, they found significant postoperative improvements in blood glucose, triglyceride levels, blood pressures and glucose tolerance tests. Gonzalez et al., (2002) found similar findings in their cohort of 12 young obese women, six of whom were randomized to large-volume liposuction, while the other six served as controls. One month postoperatively, significant decreases were noted in the blood glucose, uric acid and insulin sensitivity measured by the insulin tolerance test.

Major suction lipectomy eliminates a volume of fat and may trigger a hormonal cascade that consequently leads to further weight loss. This thesis stressed on the leptin hormone changes after major liposuction.

Aim of the Work:

This thesis aims to study the effect of large volume liposuction on the serum leptin levels and the possible effect of alteration in serum leptin on the total body weight in the postoperative period.

Obesity

Obesity is a substantial public-health crisis allover the world. The prevalence is increasing rapidly in numerous developing counteries worldwide. This growing rate represents a pandemic that needs urgent attention if its potential morbidity, mortality, and economic tolls are to be avoided (Baskin et al., 2005).

Although several definitions and classifications for degrees of obesity are accepted, the most widely accepted is the World Health Organization (WHO) criteria based on BMI. Under this convention for adults, the normal BMI is from 18.5 to 24.9 kg/m². Grade I overweight (commonly and simply called overweight) is a BMI of 25-29.9 kg/m². Grade II overweight (commonly called obesity) is a BMI of 30-39.9 kg/m². Grade III overweight (commonly called severe or morbid obesity) is a BMI greater than or equal to 40 kg/m².

The body mass index (BMI), also known as the Quetelet index, is used far

more commonly than body fat percentage to define obesity. BMI is closely correlated with the degree of body fat in most settings. BMI = weight/height2, where weight is in kilograms and height is in meters.

Obesity represents a state of excess storage of body fat. Although similar, the term overweight is puristically defined as an excess body weight for height. Although men have a body fat percentage of 15-20%, women have approximately 25-30%. Because differences in weight among individuals are only partly due to variations in body fat, body weight is a limited, though easily obtained, index of obesity.

The body fat percentage can be estimated by using the Deurenberg equation, as follows: body fat percentage = 1.2(BMI) + 0.23(age) - 10.8(sex) - 5.4, where age is in years and sex is 1 for male and 0 for female. This equation has a standard error of 4% and accounts for approximately 80% of the variation in body fat

Although BMI is typically closely correlated with percentage body fat in a curvilinear fashion, some important caveats to its interpretation apply. In mesomorphic (muscular) persons, BMIs that usually indicate overweight or mild obesity may be spurious, whereas in some persons with sarcopenia (especially among persons of Asian descent), a typically normal BMI may conceal underlying excess adiposity characterized by increased percentage fat mass and reduced muscle mass.

In view of these limitations, some authorities advocate a definition of obesity based on percentage body fat. For men, a percentage of body fat greater than 25% defines obesity, and 21-25% is borderline. For women, over 33% defines obesity, and 31-33% is borderline.

Other indices used to estimate the degree and distribution of obesity include the 4 standard skin thicknesses (ie, subscapular, triceps, biceps, and suprailiac) and various anthropometric measures, of

which waist and hip circumferences are the most important

The definition of obesity in children involves BMIs greater than the 85th (commonly used to define overweight) or the 95th (commonly used to define obesity) percentile, respectively, for age-matched and sex-matched control subjects.

Epidemiology

Approximately 100 million adults in the United States are at least overweight or obese (Baskin et al, 2005). Approximately 35% of women and 31% of men older than 19 years are obese or overweight. The numbers among children are even more imposing than these. The prevalence of obesity in children in the United States has increased markedly between the time of the National Health and Nutrition Examination Survey (NHANES) 2 and 3 trials. Approximately 20-25% of children are either overweight or obese, and the prevalence is even greater than this in some minority groups, including Pima Indians, Mexican Americans,

and African Americans. Conservative estimates suggest that the management of obesity costs approximately 100 billion dollar yearly, not including the costs of various commercial dietary and weight-loss programs (Baskin, et al., 2005).

The prevalence of obesity worldwide is increasing, particularly in the developed nations of the Northern hemisphere, such as the United States, Canada, and most countries of Europe. Available data from the Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) project suggest that at least 15% of men and 22% of women in Europe are obese (Stott, 1998).

Similar data now are being reported from many developing countries, particularly those in Asia and, to a lesser extent, those in Africa. Reports from countries such as Malaysia, Japan, Australia, New Zealand, and China detail an epidemic of obesity in the past 2-3 decades. Data from the Middle Eastern countries including Bahrain, Saudi Arabia, Egypt, Jordan, Tunisia, and Lebanon, among others, indicate this same disturbing trend,

with alarming levels of obesity often exceeding 40% and particularly worse in women (Baskin, et al., 2005).

Data from the Caribbean and from South America also highlight similar trends. Although data from Africa on this issue are scant, a clear and distinct secular trend of profoundly increased BMIs is clearly observed when people from Africa immigrate to northwestern hemispheric countries. Comparisons of these indices among Nigerians and Ghanians residing in their native countries with indices in recent immigrants to the United States show this trend poignantly (Baskin, et al., 2005).

Conservative estimates suggest that as many as 250 million people (approximately 7% of the estimated current world population) are obese. Two- to three-times more people than this are probably overweight. Although socioeconomic class and the prevalence of obesity are negatively correlated in most developed countries, including the United States, this correlation is distinctly reversed in many relatively undeveloped areas, including China, Malaysia,