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Obesity and Cardiovascular Risk in Mexico: Pathophysiology and Prevention

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Abstract

Obesity and overweight are the most common chronic condition and its prevalence is increasing. In Mexico more than 70% of adults are overweight or obese (BMI > 25) in children this entity is on the vertiginous rise. This condition is associated with an increase in cardiovascular risk, diabetes mellitus, arterial hypertension, vascular event cerebral, osteoarthritis and certain types of cancer. It is estimated that this condition costs exceed the 50 billion pesos. This systematic review aims to update the clinical and patho physiological, environmental and social aspects and its relation to cardiovascular risk that demarcates a great challenge to the social development of the nation.

Keywords: Obesity and Cardiovascular Risk; Prevention; Mexico

Introduction

One of every three deaths in Mexico today is secondary to cardiovascular disease whose most common risk factors include obesity, high blood pressure, diabetes and dyslipidemia. Nevertheless obesity is the most common underlying factor [1]. Thus prevention and treatment of these conditions must be observed a close link with its most common risk factor; obesity. Overweight or obese people represent more than two thirds of the adult population in countries like United States and mexico and are the most common reason for attention in the first level of care [1,2]. Some professional organizations now classified obesity, defined as a body mass index (BMI, weight in kilograms divided by the square of height in meters) of 30 or more, as a disease [3]. The focus of this review is approach of overweight (BMI ≥ 25) or obesity in the global and Mexican clinical context and their pathophysiological pathways, alone or in combination with other non-communicable chronic disease [4]. In the recent national survey of Mexico (2016) we found among school-age children, 17.9% (95%CI: 15.2-21.1) were overweight and 15.3% (95%CI: 12.5–18.6) Obese. This represented a total of 33.2% (5 million 253 thousand) overweight schoolchildren versus 34.4% in 2012. Prevalence predominated among 10-11years old and was 6 Percentage Points (PPs) higher in urban than in rural areas. Among adolescents, 22.4% (95%CI: 19.5, 25.6) and 13.9% (95%CI: 11.4, 16.8) presented overweight and Obesity, respectively. Compared to 2012, the overall overweight + obesity in adolescents declined just only 1 % (previous 35%) [5].

Key Factors

Environment

Chronic diseases and obesity have emerged as major health problems during the past century through shared environmental changes. Infectious diseases, which in the 19th century were the leading cause of death are now widely controlled and life expectancy has increased almost three decades since 1900 [4,5]. The factors that favor a positive energy balance and weight gain in recent decades include supplies increase and the per capita consumption of food, notably of edible foods high in calories, which often are served in large portions [5,6]; Decrease time

spent on occupational physical activity and the displacement of physical activity during leisure time with sedentary activities like watching television and the use of electronic devices, the use growing of drugs that have weight gain as a side effect and inappropriate sleep, in combination with medical innovations that have reduced mortality due to infectious diseases and the increase in life expectancy, establish the bases for the joint epidemics of chronic diseases and the obesity [7-11] (Figure 1).

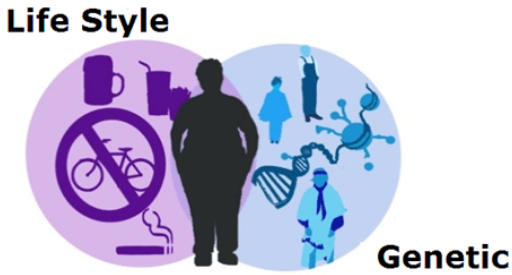

Figure 1: Genetic and environmental determinants of obesity

Genetic Determinants

Not all persons exposed to the prevailing urban and rural environments become obese, which suggests the existence of underlying genetic mechanisms that operate at the individual level. Although estimates vary, twins, family and adoption studies show that the rate of heritability of BMI is high, ranging from 40 to 70% [12]. Eleven rare monogenic forms of obesity are now recognized, including a deficiency of leptin and receptors melanocortin, which are mainly expressed in the hypothalamus and are involved in the neural circuits that regulate the homeostasis of the energy (Figure 2). Mutations heterozygotes in the melanocortin-4 receptor gene are currently the most common cause of obesity monogenic, appearing in 2-5% of children with severe obesity [13,14]. Appetite comes to the point of satiety.

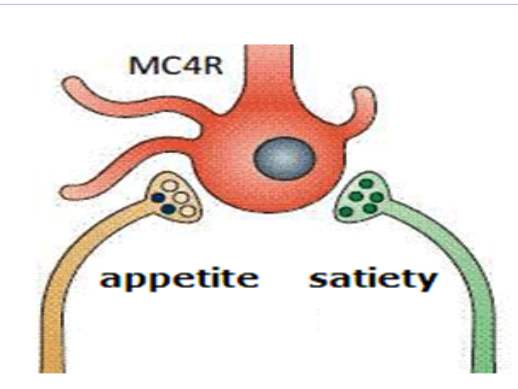

Figure 2: Melanocortin receptor 4, directly related to the appetite-satiety axis

A strategy widely used to discover polygenetic mechanisms that confer susceptibility to common obesity involves detection of whole genome in large samples in order to identify single nucleotide polymorphisms associated with the BMI and other obesity-related traits. More than 300 loci have been identified in genome wide association studies, though collectively these loci represent less than 5% of individual variation in BMI and traits of adiposity [13]. The most prominent signs using this approach are variants of FTO gene; People who carry one or two copies of the risk allele have an increase of 1.2 kg or 3 kg of weight, respectively, compared with people without the whole exome allele [13]. Copies and the sequencing of the entire genome offer the possibility of identifying new targets best and molecular markers for predicting risk.

Changes in gene transcription and translation through environmental influences can occur without changes in the sequence of DNA nucleotides. All the epigenome association studies are clarifying prenatal and postnatal exposures that may influence the results of the metabolic [14,15]. Health effects epigenetic can, therefore, explain the additional differences among people in BMI and obesity phenotypic traits [12].

Energy Imbalance

Genes and the environment interact in a complex system that regulates energy balance, the weight and related physiological processes [13,14](Figure 1). Two sets of neurons in the arcuate nucleus hypothalamic that are distressed or excited by the neuropeptides circulating hormones control the energy balance regulating food intake and energy expenditure. Short- and long-term energy balance is controlled through a coordinated network of central mechanisms and peripheral signals arising from the Microbiome and cells in adipose tissue, stomach, pancreas and other organs [14]. Regions of the brain out of the hypothalamus contributes to the regulation of energy balance through the signal's sensory input, cognitive processes, the hedonic effects of food consumption, memory, and attention [14].

Reduce food intake or increase physical activity leads to a negative energy balance and a cascade of adaptation mechanisms countervailing power and peripherals that preserve the functions vitals [15,16]. Seen clinically, these effects can be associated with related reductions in energy expenditure at rest, concern for food, and many other processes metabolic and psychological that depend on the magnitude and duration of caloric restriction [17,18]. An increase in the Central signals orexigenic can explain subtle and often not appreciated increased the regulation of appetite and food intake that limits the degree of expected weight loss that is associated with interventions such as programs of exercises [19].

These well-established physiological and metabolic effects that appear during weight loss can be kept in the reduction weight state [16,17]. Although the magnitude and underlying mechanisms of these effects in humans remain unclear, the implication is that people who are not obese may not be physiological and metabolically identical to their counterparts who never were obese [16,17]. High relapse rates are in accordance with this point of view and are consistent with the concept of obesity as a chronic disease that requires monitoring long term and weight control.

Pathophysiological Pathways

Excess of fatty tissue in the obese evolves gradually over time, with a positive energy balance in the long term. The accumulation of lipids, mainly triglycerides in adipose tissue occurs along with volume increases in skeletal muscle, liver and other organs and tissues; Excess weight in people with overweight or obesity include varying proportions of these organs and tissues [20]. Obese person with permanent weight, compared to a person without overweight or obese, therefore has a greater mass of fat and lean, together with a greater expenditure of energy at rest, cardiac output and blood pressure and greater mass of pancreatic β cells [20,21]. The secretion of insulin in the fasting state and after glucose load increases linearly with BMI [22].

The excess of lipids is divided into many compartments of the body. Subcutaneous adipose tissue contains most of the lipid stored in a variety of anatomical sites that differ in their metabolic and physiological characteristics [23]. The majority of adipocytes in the subcutaneous adipose tissue are called white, because of stored triglycerides.

Relatively small and variable amounts of beige and grey/brown thermogenic adipocytes are also present in adults [24] (Figure 3). Obesity is accompanied by increases in macrophages and other immune cells in adipose tissue, in part due to the redevelopment of tissues in response to apoptosis of the adipocytes [25]. These immune cells secrete pro-inflammatory cytokines that contribute to insulin resistance, endothelial dysfunction and oxidative stress, which often is present in patients with obesity.

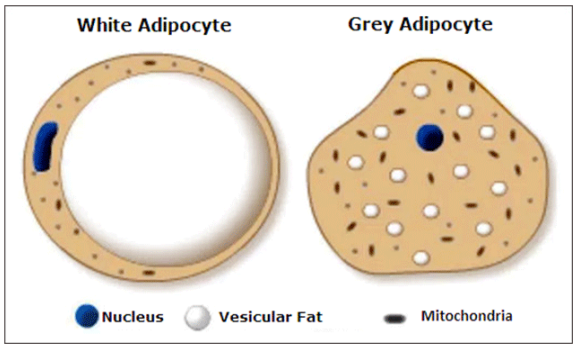

Figure 3: White and Grey or Brown Fat

Visceral adipose tissue is a smaller swap for lipids than subcutaneous adipose tissue, with omental and mesenteric fat mechanically linked to many of the metabolic disturbances and adverse outcomes associated with obesity [23,24]. The adipose tissue surrounds the kidney and the increase in blood pressure with renal compression can contribute to high blood pressure frequently observed in obese patients obese [21]. Obesity tends to be accompanied by an increase in pharyngeal soft tissue, that it can block the airway during sleep, causing an obstructive sleep apnea. Excess adiposity also imposes a mechanical load on joints, making obesity a risk factor for the development of osteoarthritis [26,27].

An increase in intra-abdominal pressure supposedly explains elevated risks of disease by gastro esophageal reflux, Barrett's esophagus, and esophageal adenocarcinoma among people with overweight or obesity [28].

Metabolic Effects

Adipocytes synthesize adipocytokines (cell signaling proteins) and hormones, whose rates of secretion and effects are influenced by the distribution and the amount of adipose tissue present [24] (Figure 4).

The excessive secretion of proinflammatory adipokine by adipocytes and macrophages in adipose tissue leads to a systemic inflammatory condition of low grade in some people with obesity [24].

The hydrolysis of triglycerides in adipocytes releases free fatty acids, which are then transported in plasma to sites where they can be useful metabolically. Plasma free fatty acid levels are often high in patients with obesity, reflecting several sources including the enlarged adipose tissue mass [24].

In addition to being in the adipose tissue, lipids also found in Liposomes, which are small cytoplasmic organelles in the proximity of the mitochondria in many types of cells [29]. With excess adiposity, liposomes in hepatocytes they can increase in size (steatosis), forming large vacuoles which, accompanied by a series of pathological States, including liver disease, fat non-alcoholic steatohepatitis and cirrhosis. The accumulation of lipid intermediates in excess (eg: ceramides) in some non-adipose tissues can lead to cellular dysfunction and apoptosis lipotoxicity [24].

High levels of free fatty acids, inflammatory cytokines, and lipid intermediates in non-adipose tissues contribute to the alteration of the signaling of insulin and the State of resistance to insulin that is present in many patients with overweight or obesity [24, 30, 31]. The insulin resistance and atherogenesis are also strongly linked to excess intra-abdominal adipose tissue [24,31] (Figure 5).

This constellation of metabolic and anatomical findings is one of several underlying pathophysiological mechanisms to the dyslipidemia of obesity (elevated levels of plasma triglycerides in fasting and cholesterol of low density lipoprotein and low levels) high-density lipoprotein cholesterol), type 2 diabetes, osteoarthritis and obesity-related liver disease. Elevated levels of bioavailability of growth factor similar to the insulin 1 and other tumors, promoting molecules have been implicated in the development of some cancers [32].

The chronic over activity of the sympathetic nervous system is present in some patients with obesity and can be explained in part by multiple pathophysiologic processes, including blood pressure high [21]. Heart disease, accidents stroke and chronic kidney disease have as main pathophysiological mechanisms group of findings associated with insulin resistance, dyslipidemia associated with obesity and type 2 diabetes and high blood pressure.

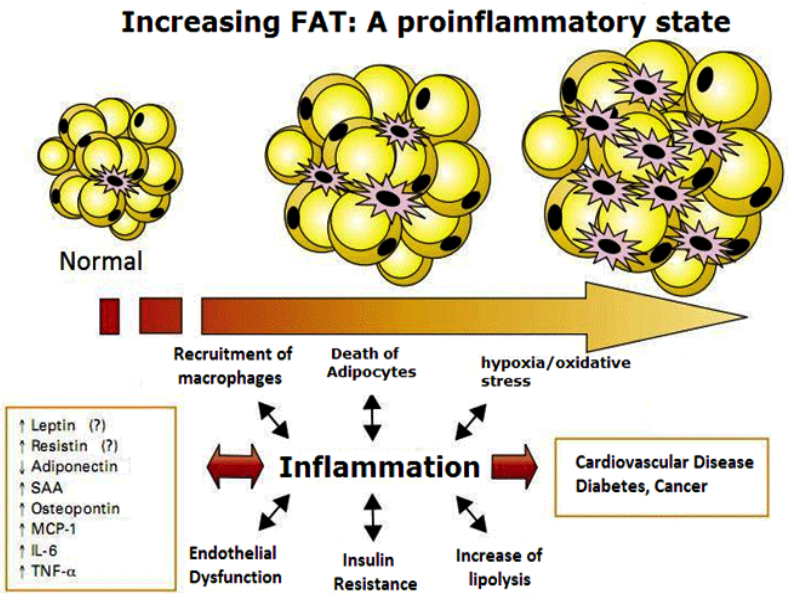

Figure 4: Obesity- a pro inflammatory state

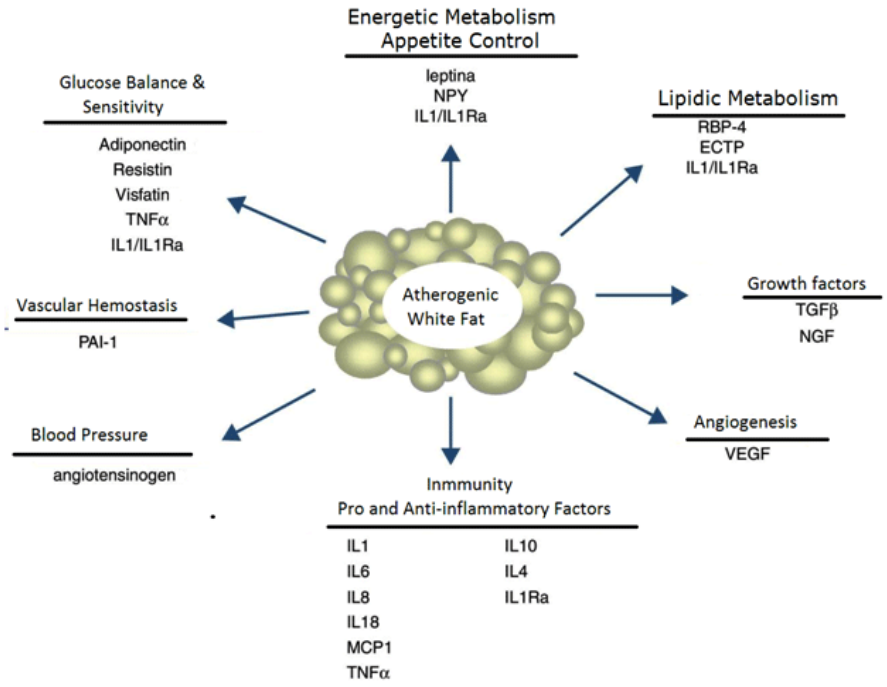

Figure 5: Fat white mainly intra-abdominal generating of multiple disorders

Psychological Effects

Obesity is associated with an increase in the prevalence of mood, anxiety and other psychiatric disorders, especially among people with severe obesity and those who seek the bariatric surgery [33,34]. Causal pathways between obesity and disorders psychiatric can be bidirectionals [35]. In addition, the medications used to treat bipolar disorder, major depression and some psychotic disorders may be accompanied by considerable weight gain [9,33].

Response to Weight Loss

When it induces a negative energy balance by reducing food intake, increasing activity levels, or both, the thermodynamic prediction models accurately defined the path of weight loss in patients adherents [35,36]. Most of patients reach a nadir of weight loss earlier than expected by these models, after only several months, and gradually increase in weight later. Regained weight is related to a lower adherence to diet and activity requirements and increasingly recognized endogenous compensatory mechanisms [16,37].

The loss of moderate weight, defined as a reduction of 5 to 10% in the baseline weight, is associated with clinically significant improvements in metabolic risk factors related to obesity and disorders coexistentes [9,38,39]. A 5% weight loss improves the function of pancreatic β cells and the sensitivity of liver and skeletal muscle insulin; A relative weight loss wholesale leads to improvements graduated in key disorders tissue adipose [40,41]. A year, patients had a weight loss average of 8.6 per cent from the baseline, which was accompanied by significant reductions in systolic blood pressure and diastolic (6.8 and 3.0 mm Hg, respectively) and triglyceride levels (30.3 mg per deciliter [0.34 mmol per liter]) and (from 0.64%) glycosylated hemoglobin. A response graduated for these sensitive measures the weight, with further loss of weight accompanied by greater improvements were observed [42].

Moderate weight loss can result in the prevention of disease in people at high risk. Overweight or obesity and impaired glucose tolerance patients who received an intensive lifestyle intervention in the Diabetes prevention program had a weight loss average of 5.6 kg at 2.8 years and a relative reduction of 58% of risk to developed [43,44].

Losses average of 16 to 32% of the baseline weight produced by weight loss surgery in patients with severe obesity can lead to remission of the disease, including remission of diabetes type 2 in patients undergoing surgery, in particular the gastric bypass [45-50]. have also shown significant reductions in mortality from all causes in observational studies of patients treated surgically [51,52].

Although weight loss is an effective therapeutic measure of broad action, not all risk factors and chronic disease States respond equally bien [38,39-42]. Severe obstructive sleep apnea, for example, improves but rarely forwards fully in response to treatments for weight loss, including Bariatric Surgery [26].

On the other hand, the moderate weight loss beneficial clinical effects achieved with intensive intervention in the style did not reduce the morbidity and mortality associated with cardiovascular disease after 9.6 years in the study look towards a head [53]. Well established medical therapies should be used with weight loss to achieve good control of coexisting conditions linked to obesity. Similarly, the symptoms of some psychiatric disorders can improve with weight loss, but complementary psychiatric care is critical, particularly in people with moderate or severe disorders [33,54]. For example, shown that the complementary care is invaluable for improving mental health and eating behaviours, such as the binge eating syndrome [34].

Clinical Approach

The phenotypic characteristics of the obese are complex, and some patients have no apparent cardiometabolic effects, a phenomenon that has been called the "metabolically healthy" obese state [55]. The groups of findings related to the insulin resistance with increased intra-abdominal subcutaneous fat mass and the upper part of the body are consistent with the diagnosis of a metabolic syndrome [24,31].

Although the BMI is a good indicator of adiposity at group level, each patient's risk can Stratify further on the basis of a personal medical history and family, a history psychiatric and blood studies, as well as a behavioural history that includes information about physical activity, nutrition, and behavior food [33,34]. The waist circumference is also a useful measure of intra-abdominal and upper part of the subcutaneous adipose tissue body, and some guidelines include it as a marker of risk in addition to or instead of the body mass index [31,39].

Cardiovascular Risk Evaluation

One of the aspects most relevant consequences of obesity is its impact as a cardiovascular risk factor (Figure 6).

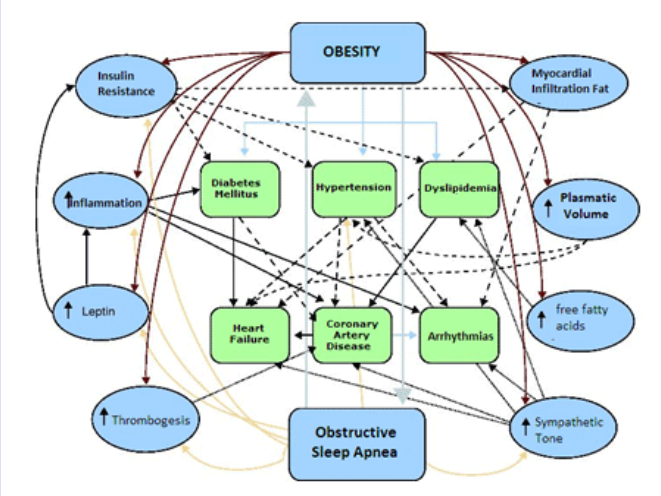

Figure 6: Cardiovascular and metabolic risk in the obese

The recognition of the Adipocyte as an endocrine cell activates and not only had a simple repository of lipid revolutionized the understanding of the underlying mechanisms that promote

and develop cardiovascular risk factors. Thus, the obese patient generates insulin resistance, favors high blood pressure and diabetes, Endothelial dysfunction, diabetes, thrombogenic disorder and disorders in lipid metabolism, stimulates abnormal growth of extracellular matrix, metalloproteins and promotes infiltration of lipids in tissue, skeletal muscle, liver and even promotes hypertrophy, myocardial and flattering diastolic dysfunction of cardiac arrhythmias.

Thus, the adipose tissue synthesized and secret molecules biologically active that they affect cardiovascular risk factors. These chemical messengers including adiponectin, resistin, leptin, Inhibitor of the activator of plasminogen-1, Interleukin-6 and tumoral necrosis factor. In individuals with overweight and obesity, weight loss may improve sensitivity to insulin, leading to the reduction of risk factors for cardiovascular diseases and, accordingly, the potential for cardiovascular events.

Agents that improve insulin sensitivity, as thiazolidinedione have proven to reduce visceral obesity. Decreases in visceral adipose tissue contribute to improvements in insulin sensitivity and blood pressure and weight loss reduces serum levels of triglycerides and low-density lipoprotein cholesterol while increasing serum levels of high density lipoprotein cholesterol. Reduction of risk factors suggests that the development of cardiovascular disease will be reduced by improving insulin sensitivity and weight loss.

Treatment

Treatments must be aligned with the seriousness of the overweight, co-existing chronic illnesses and functional limitations. There are useful guidelines to evaluate the health risks and the options of treatment of a patient individual [38, 39, 56]. Main with sufficient supporting evidence-based treatment options are intervention in the lifestyle, drug therapy and the Bariatric Surgery [9,38, 39, 57].

The Lifestyle Intervention

Lifestyle interventions designed to change eating behaviors and physical activity are the first choice for the weight management, given its low cost and minimum risk of complications [39]. The goal for patients who have overweight or obesity is to improve the health and quality of life by achieving and maintaining moderate weight loss. Extensive research led to the current recommendations that patients receive advice behavior of high intensity, with 14 or more trips in 6 months [39].

A comprehensive program, carried out by a trained interventionist, resulting in a loss of average weight of 5 to 8% 39 and approximately 60 to 65% of patients lost 5% or more of the initial weight (weight loss 1 year high in lifestyle interventions intensity or drug therapy combined with counseling of low to moderate intensity lifestyle).

50:50 Mexican Institute of Social Security Program

Behavioral therapy, core of the lifestyle intervention, provides the patients techniques to adopt dietary recommendations and activity. These recommendations include the regular recording of food intake, physical activity and weight. This task can be facilitated by smart phones applications, activity meters and scales with cellular connection [39,58-63]. Patients review their progress approximately once a week with a trained interventionist providing stimulus and targets and troubleshooting instructions.

Fifty-fifty program was born from the initiative of the Foundation SHE, promoted by Dr. Valentín Fuster, in order to improve health comprehensively in adults by modifying their health habits. The scientific study, which shows that the program has a positive impact on cardiovascular health, has counted with the support of the Spanish Agency of consumption, food safety and nutrition (AECOSAN) of the Ministry of health, social services and equality, in the framework of the NAOS strategy and the Observatory of nutrition and obesity study. In the IMSS this program started with promising results.

Education in Children of Mexico

SI Program of Dr. Valentín Fuster consisted of education to pre-school children of 3 to 5 years in Spain, achieving major changes in habits and customs in favor of nutrition and body weight [39]. The IMSS is preparing in collaboration with Spain a similar program in Mexico. The program aims to improve the overall health in adults helping them to correct their health habits and self-manage the major risk factors for cardiovascular disease: not healthy eating, Overweight/obesity, physical inactivity, smoking and high blood pressure [39].

Barriers to Treatment

Only a small fraction of patients receives some of these three kinds of treatments. Barriers to care include slow recognition by the health care providers that obesity requires a long-term management, inadequate training of physicians in nutrition and obesity, a refund limited the full range of the lack of effective and affordable lifestyle programs and treatments. While Bariatric Surgery is a treatment option for improving health of level (i.e., with improvements based on data from randomized trials or meta-analyses) [39]. The hope is to create a growing national, multidisciplinary network of medical professionals with high level of training and certification in the treatment of obesity surpassing some of these impediments to effective patient care [64-66].

Conclusion

The creation of conditions for healthy living in our modern environment, including the prevention of obesity, is one of the greatest challenges for humanity. Doctors alone, taking care to affected patients, cannot handle all the roads that lead to the genesis of excess adiposity, but can proceed with the knowledge that management interventions described here will benefit patients that they receive. Much more effort should be devoted both to the prevention and treatment of obesity as part of the global campaign to control the epidemic of chronic diseases.

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