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The need for pharmacological treatment in obesity

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ABSTRACT

The growing prevalence of overweight and obese populations has reached epidemic proportions worldwide. The principal causes of this increase are high dietary fat intake and reduction of physical activity, but there are also environmental and genetic factors. Overweight is described by a body mass index between 25.0 and 29.9 kg/m^2, while a body mass index equal to or higher than 30 kg/m^2 indicates obesity. Obesity reduces life expectancy and is a risk factor for several chronic diseases such as type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, or sleep apnea. Therefore, it is considered a public health problem and its treatment is imperative. The treatment of overweight and obesity is based in reducing body weight. The initial treatment is based on lifestyle interventions by dietary therapy, increased physical activity, and behavioral therapy. If lifestyle interventions are not enough to achieve the weight loss goals, pharmacologic therapy is recommended. The pharmacologic agents available reduce dietary intake by increasing signals of satiety on the central nervous system, reducing

RESUMEN

La prevalencia del sobrepeso y obesidad ha incrementado hasta alcanzar proporciones epidémicas en todo el mundo. Las principales causas son la elevada ingesta de grasas, y la reducción en la actividad física, aunque también existen factores ambientales y genéticos. El sobrepeso está descrito por un índice de masa corporal entre 25 y 29.9 kg/m^2, mientras que cuando es igual o superior a 30 kg/m^2 indica obesidad. La obesidad reduce la esperanza de vida y es un factor de riesgo para enfermedades crónicas como la diabetes de tipo 2, hipertensión, enfermedad cardiovascular, o apnea del sueño. Por lo tanto, se considera un problema de salud pública y su tratamiento es necesario. El tratamiento del sobrepeso y obesidad se basa en la reducción del peso corporal. El tratamiento inicial consiste en cambios en el estilo de vida con terapia alimentaria, incremento de actividad física y terapia de comportamiento. Si el cambio de estilo de vida no es suficiente para conseguir la reducción de peso se recomienda la terapia farmacológica. Los fármacos disponibles actúan reduciendo la ingesta de alimentos, la absorción de

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absorption of dietary fat, and increasing energy expenditure. Finally, patients with extreme obesity or obesity with serious weight-related health problems are considered for bariatric surgery. (REV MEX ENDOCRINOL METAB NUTR. 2016;3:24-33)

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grasas e incrementando el gasto energético. Finalmente, los pacientes con obesidad extrema o con obesidad y problemas serios de salud relacionados con el peso son considerados para tratamiento con cirugía bariátrica.

Palabras clave: Obesidad. Pérdida de peso. Lorcaserina. Fentermina. Topiramato. Liraglutide.

INTRODUCTION

During the last decades, the prevalences of overweight and obesity have reached epidemic proportions worldwide. Between 1980 and 2013, the number of overweight and obese persons increased from 857 million to 2.1 billion, with an increase in prevalence of 27.5% for adults and 47.1% for children[1]. The highest rates of obesity have been reported in the Pacific Islands and the lowest ones in Asia[2]. In 2013, Samoa presented the highest prevalence of obesity for women (69.1%) and Tonga showed the highest one for men (52.4%). On the contrary, India had the lowest rates of obesity of men (3.7%) and women (4.2%), followed by China, with 3.8% of men and 5.0% of obese women[1].

Even age patterns differed in men and women between developing and developed countries. At all ages, prevalence of overweight and obesity in 2013 was higher in developed than in developing countries (Fig. 1). Sixty-two percent of the world's obese individuals live in developed countries, with the USA leading the list with 13% of obese people worldwide. It is estimated that in 2015, 75% of adults and around 24% of children and teenagers in the USA were obese or overweight[3].

The increase in the prevalence of obesity worldwide has been attributed to an increased intake of dietary fat, low intake of fruits and vegetables, and a reduction of physical activity[4-6], but there is also environmental and genetic predisposition to develop obesity[2]. Nowadays, obesity is considered a very complex illness determined by biological, but also psychological, social, economic, and cultural factors. Psychological disorders, such as depression, anxiety, or eating disorders, may make it difficult to control consumption of food and maintain a healthy weight[7]. There is also the hypothesis that social networks may have an influence in the obesity epidemic. Having obese social contacts may change specific behaviors or the tolerance for being obese. Also, some psychological imitation might occur, and weight gain in one person might influence weight gain in others[8]. The socioeconomic status of people, but also the economic development of the country, is also highly related with obesity. People with a high socioeconomic status in lower-income countries are more likely to be obese due to consumption of high-calorie food and avoidance of physically extenuating labor. Conversely, in high-income countries, those with a higher socioeconomic status are less likely to be obese due to healthy eating and regular exercise[9].

Moreover, obesity is considered a public health problem since it reduces life expectancy and it is a risk factor for developing cardiovascular diseases, some types of cancer, and type 2 diabetes. In 2010, overweight and obesity were estimated to cause 3.4 million deaths, 3.9% of years of life lost, and 3.9% of disability-adjusted life-years worldwide[1].

DEFINITION OF OBESITY

Obesity is a chronic disorder produced by multiple factors that result in having excess body fat. The World Health Organization (WHO) adopted body mass index (BMI) as a measure of total body fat; BMI is calculated by dividing the body weight in kilograms (kg) by the square of the height in meters (m^2)[10].

Adults of 18 years and older are considered obese when their BMI is ≥ 30 kg/m^2, while a BMI between 25.0 and 29.99 kg/m^2 indicates overweight[1]. The criteria in children for overweight consider a BMI between the age-specific 85th and 94th percentile and for obesity as at or above 95th BMI percentile[1,11].

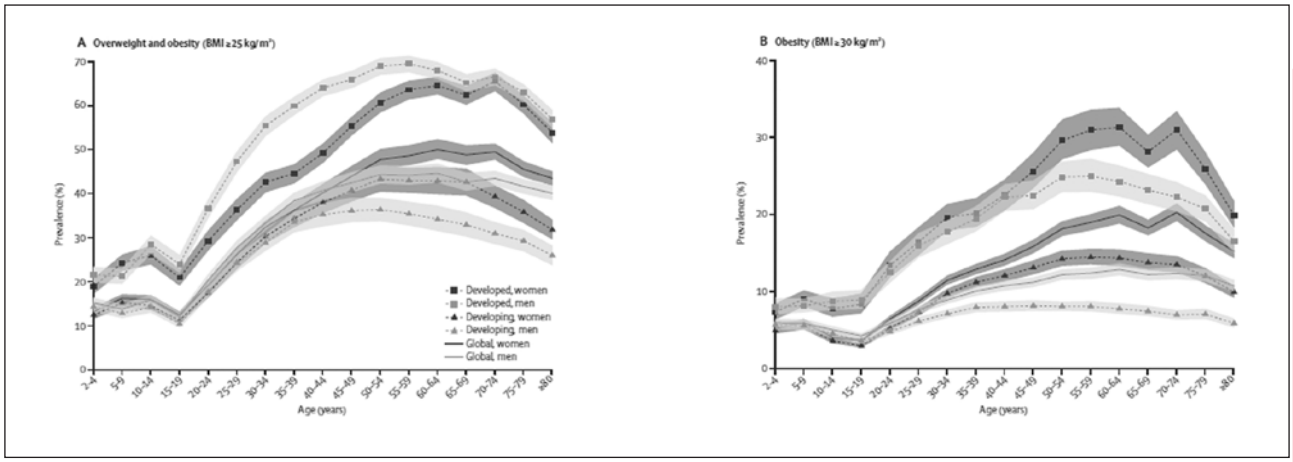

Figure 1. Prevalence of overweight and obesity and obesity alone by age, sex, and development stage of the country. BMI: body mass index[1].

According to the mechanism of adipose tissue to increase its storage of lipids, obesity can be classified as hypertrophic or hyperplastic[12,13]. Hypertrophic obesity is characteristic in adults and results from a normal number of fat cells that increase in size. Usually, individuals that were thin or average weight when they were young become less active when they get older and gain weight at age 30-40, becoming overweight or moderately obese[13]. Hyperplasic obesity is a long-term type of obesity characterized by a greater number of adipocytes than normal that are also larger than normal. This type of obesity usually begins at an early age and is associated with a high weight gain during puberty. In non-obese children, the number of fat cells triples or quadruples between birth and two years and remains stable until puberty, when there is a further increase in number. However, obese children also increase the number of adipocytes between two years and puberty. After puberty, the number of fat cells remains stable during all life[13].

The severity of obesity can be accurately classified by BMI. According to the Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, obesity class 1 corresponds to a BMI between 30.0 and 34.9 kg/m^2, BMI for obesity class 2 is between 35.0 and 39.9 kg/m^2, and individuals with BMI ≥ 40 kg/m^2 present extreme obesity (class 3), previously known as morbid obesity[14]. Other methods used to classify obesity are rather based on a more comprehensive appreciation of mild, significant, severe, or terminal complications or comorbidities on physical and psychological spheres, such as the Edmonton Obesity Staging System[15], which consists of five different stages based on medical history, clinical and functional assessments, and simple routine diagnostic investigations.

RELATED DISEASES

Obesity has been associated with an increased risk of death by at least 2-3 times of that of the normal-weight population. The risk of death also increases among overweight persons at age of 50 years by 20-40%[16]. In fact, overweight and obesity substantially increase the risk of numerous chronic diseases[14,17].

The prevalence of diabetes has increased considerably during the last decades[18], which is closely linked to the increase of obesity. About 90% of type 2 diabetes can be attributed to excess weight, and the principal cause for impaired glucose tolerance is obesity and the associated metabolic syndrome[5]. There are several mechanisms that link obesity with type 2 diabetes development[19]. An increased production of adipokines associated with obesity and metabolic syndrome leads to insulin resistance and other biochemical alterations of metabolites[20]. Ectopic fat deposition, particularly in liver, heart, pancreas, and blood, has also been related with insulin resistance[21], and an impaired adipose mitochondrial function decreases insulin sensitivity and produces β-cell dysfunction, which

leads to dysregulation of homeostasis of adipocyte tissue that may also cause several metabolic diseases such as insulin resistance and type 2 diabetes[22].

Obese people also develop dyslipidemia, which is also related with insulin resistance. As a result of insulin resistance, there is an increased hepatic synthesis of very low density lipoproteins (VLDL) and impaired lipoprotein lipase, which leads to a reduced high density lipoprotein (HDL) and increased triglycerides[17,23].

The risk of cardiovascular disease is considerably greater among obese people, and the incidence of hypertension is five times higher than the incidence among normal-weight populations[5]. There are evidences that not only the total body fat but also the distribution of fat in the body is highly related with cardiovascular disease and hypertension. Thus, high waist fat distribution assessed by waist circumference has been associated with high rates of myocardial infarction[24].

Even though the relationship between obesity and hypertension is well established, the mechanisms of this relation are still not clear. One possible mechanism is the activation of the sympathetic nervous system as a result of a high-caloric intake. Obese individuals also present a higher blood pressure as a result of an expanded extracellular fluid volume, which is caused by arterial pressure control mechanism of diuresis and natriuresis. The increase in plasma of renin activity, angiotensinogen, angiotensin II, and aldosterone values during obesity, or the altered profile of vascular function promoted by insulin resistance and inflammation, can also cause hypertension. And another possible link between obesity and hypertension is hyperleptinemia[25]. Besides, hyperleptinemia as well as increased concentrations of C-reactive protein (CRP) has also been associated with an increased risk of major cardiovascular events[26]. Moreover, obese and overweight individuals with higher blood pressure often develop left ventricular chamber dilatation, other structural abnormalities, and left atrial enlargement that not only increase the risk of heart failure but also of atrial fibrillation and morbid complications (Fig. 2)[27,28].

Other complications associated with obesity are sleep apnea and respiratory problems. Sleep apnea consists of repeated episodes of obstructive apnea and hypopnea during sleep as well as daytime sleepiness or altered cardiopulmonary function[29]. Obese individuals have a decreased expiratory reserve volume and functional reserve capacity, respiratory muscle inefficiency, and closure of peripheral lung units, which cause sleep apnea and alveolar hypoventilation. Hence, obesity is a major cause of respiratory insufficiency and pulmonary hypertension in patients with obstructive sleep apnea[30].

Osteoarthritis, gastrointestinal abnormalities, reproductive disease, incidence of some cancers, and psychosocial problems are other complications associated with obesity[17].

BENEFITS OF WEIGHT LOSS

The treatment of overweight and obesity is a priority for the public health, owing to the major health risks and diseases associated with obesity, which reduce life expectancy and have an associated high healthcare cost[3].

The objective for treatment of overweight and obesity is to reduce body weight. Weight loss, and especially a reduction in waist circumference, has positive effects on the risk for diabetes, cardiovascular diseases, hypertension, and insulin resistance; it also reduces serum triglyceride levels and increases HDL cholesterol levels. Modest weight losses achieved with lifestyle or metformin have been related with reductions in diabetes incidence in 10 years by 34 and 18%, respectively[31]. Reduction in weight also reduces diabetes-related complications such as cardiovascular disease risk factors including hypertension and dysplipidemia[32]. A 5-10% weight loss has been associated with significant improvements in cardiovascular disease risk factors at one year, and the benefits can be greater with larger weight losses[33]. Obese women older than 65 years that achieve significant weight reductions can experience significant reductions in systolic blood pressure, HbA_{1c} and CRP[34]. Severely obese patients who have received gastric bypass surgery achieve rapid weight loss associated with diabetes remissions and a reduction of cardiovascular disease risk[35]. Moreover, weight loss also consistently improves psychological outcomes such as body image and health-related quality of life[36,37].

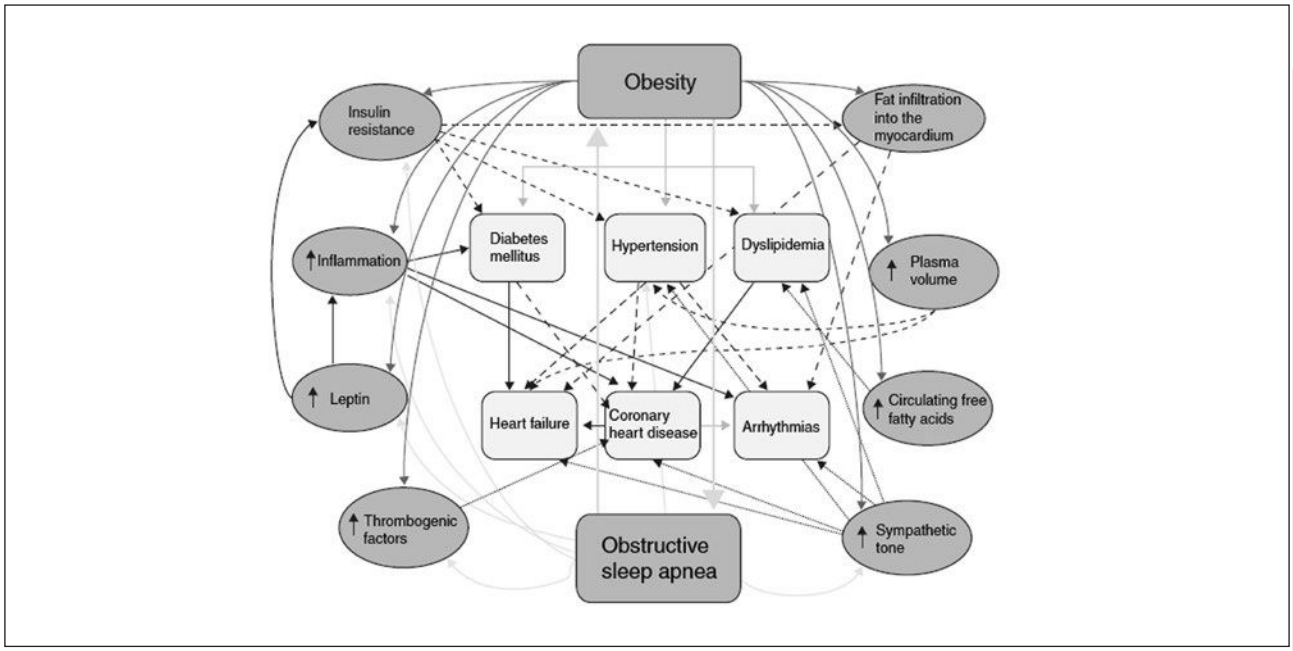

Figure 2. Pathophysiology of obesity and cardiovascular disease. The different physiopathological mechanisms by which obesity is associated with cardiovascular disease are complex and are not limited to factors such as diabetes mellitus type 2, hypertension, or dyslipidemia. Other factors with an indirect interaction have been described, such as subclinical inflammation, neurohormonal activation with increased sympathetic tone, elevated leptin and insulin concentrations, obstructive sleep apnea, increased free fatty acid turnover, and intramyocardial and subepicardial fat deposition[28].

PARADIGM OF TREATMENT

In order to provide the most appropriate treatment, obese and overweight patients at risk for health complications should receive a complete physical and clinical examination to determine the possible causes of weight gain, such as thyroid dysfunction or medication-induced weight gain, besides the assessment of BMI, waist circumference, and overall medical risk[38].

The initial treatment to achieve a reduction of body weight is based on lifestyle intervention by dietary therapy and increased physical activity, as well as behavioral therapy to reinforce weight-reduction behaviors. When lifestyle changes alone are insufficient, medication or even bariatric surgery, especially for morbidly obese patients or obese patients with multiple comorbidities, may be used. However, appropriate candidates for bariatric surgery must also be committed to long-term lifestyle changes[3]. There are evidences that medication should be used in combination with lifestyle modifications rather than as single therapy. A study performed with obese adults who randomly received sibutramine alone, lifestyle modification counseling alone, or sibutramine plus lifestyle modification counseling demonstrated that the combination of medication and lifestyle modifications resulted in more weight loss than either medication or lifestyle intervention alone[39,40]. Moreover, the setting of more realistic weight loss should reduce the frustration due to the achievement of modest weight reductions. However, patients who are treated with adjunctive pharmacotherapy should be advised of the risks and benefits of drug therapy, including the adverse events and the temporary and modest nature of the weight loss that can be achieved with these agents[41].

Lifestyle interventions

Lifestyle interventions include dietary therapy, increased physical activity, and behavioral therapy. Dietary therapy is based in reducing total calorie intake in order to induce a state of negative energy balance.

Table 1. Agents suspended of licensing as anti-obesity drugs[65]

Drug	Year	Reason for suspension
Dinitrophenol	1938	Dermatitis, neuropathy, agranulocytosis, visual impairment, death
Aminorex	1968	Chronic pulmonary hypertension
Amphetamines (schedule III)	1971	Addiction, hypertension, myocardial toxicity
Fenfluramine/ dexfenfluramine alone or in combination with phentermine	1997	Valvular heart disease
Phenylpropanolamine	2000	Hemorrhagic stroke
Rimonabant	2009	Psychiatric disorders, depression, suicidal ideation
Sibutramine	2010	Risk of major cardiovascular events

A reduction of dietary fat is necessary, but also a reduced intake of carbohydrates and an overall caloric restriction[3]. To induce the negative energy balance, a reduced calorie intake can be prescribed of 1,200-1,500 kcal/day for women and 1,500-1,800 kcal/day for men, or a 500-750 kcal/day energy deficit[42]. However, calorie-restricting diets lead to short-term weight loss but are rarely successful over the long term[43].

Increased physical activity has as initial goal the participation of the patient in moderate physical activity for 30-45 minutes, 3-5 days per week. Some of the results of physical activity are moderate reduction of body weight, an increase of cardiorespiratory fitness, and a reduction of the risk for cardiovascular disease as well. It also protects against the loss of lean body mass, reduces obesity-related cardiometabolic health risks, and evokes sensations of well-being. The combination of low-calorie diet and increased physical activity results in greater weight loss and reduction of abdominal fat, and improves cardiorespiratory fitness[42,44].

The strategies to reinforce weight reduction behaviors constitute the behavioral therapy. This therapy comprises strategies to overcome barriers to achieve weight reduction goals by helping patients identify cues that trigger inappropriate eating. The treatment includes self-monitoring, such as keeping food and activity records, controlling cues associated with eating, nutrition education, slower eating habits, and problem solving. There are also cognitive components of the therapy to correct negative thoughts that occur when goals are not achieved and help patients to set realistic goals for weight and behavior change[45].

Pharmacologic therapy

The pharmacologic agents available mainly act by impairing dietary intake by the suppression of appetite, targeting the noradrenergic, dopaminergic, and serotonergic receptor systems in hypothalamus, act peripherally to impair dietary absorption and reduce absorption of dietary fat, and increase energy expenditure by stimulating thermogenesis.

Sibutramine is a norepinephrine and serotonin reuptake inhibitor that suppresses appetite and stimulates thermogenesis[46]. It was approved in November 1997 by the US Food and Drug Administration (FDA) for weight loss and maintenance of weight loss in obese people as well as in certain overweight people with other risks for heart disease. The Sibutramine Trial of Obesity Reduction and Maintenance (STORM) demonstrated the efficacy of sibutramine in the reduction and maintenance of weight loss, with a maintained weight loss ≥ 5% at two years in 43% of participants in the sibutramine group versus 16% of patients in the placebo group[47]. This agent also improved the lipid profile and reduced blood glucose levels in type 2 diabetes patients[48]. However, patients treated with sibutramine showed increased risk of serious cardiovascular events, and in August 2010 the FDA withdrew sibutramine from the US market (Table 1)[49].

The sympathomimetic amines are derivatives of amphetamine that suppress hunger signals and appetite by stimulating neurons to maintain high concentrations of dopamine and norepinephrine. The use of the derivatives of amphetamines is contraindicated in patients with cardiovascular disease, hypertension, and other weight-related complications, and hence the use of these agents in obese patients with some comorbidities is difficult[3]. Some of these agents approved by the FDA in 1959 as short-term adjuncts in the management of obesity are phendimetrazine and

Table 2. Summary of randomized placebo-controlled anti-obesity drug trials[65]

Drug	Reference	N (T2D)	BMI (mean)	Age (mean)	1-year Δ%WL (mean)	% with >5% WL (vs. placebo)	Frequent side effects	Uncommon side effects
Lorcaserin	Smith, et al. 2010, (BLOOM)	3,182 (0)	36.2	44.1	3.7%	45% vs. 20%	Dry mouth Fatigue	Nausea Urinary tract infection
Lorcaserin	Fidler, et al. 2011, (BLOSSOM)	4,008 (0)	35.9	43.8	3.0%	47% vs. 25%	Dizziness Headache	Constipation/ diarrhoea Hypoglycaemia (in patients with T2D)
Lorcaserin	O'Neil, et al. 2012, (BLOOM-DM)	604 (604)	36.0	52.4	3.5%	45% vs. 16%		
Phentermine/ topiramate	Allison, et al. 2012, (EQUIP)	1,267 (0)	42.2	42.6	9.4%	67% vs. 17%	Paraesthesia Dry mouth	Palpitations Disturbances in attention
Phentermine/ topiramate	Gadde, et al. 2011, (CONQUERI	2,487 (393)	36.6	51.1	8.6%	70% vs. 21%	Constipation Headache Dysgeusia Insomnia Dizziness	Alopecia Diarrhoea Anxiety and irritability Depression/fatigue Blurred vision Glaucoma
Liraglutide	Astrup, et al. 2012	398 (21)	34.8	45.9	4.9%	73% vs. 28%	Nausea Vomiting	Pancreatitis
Liraglutide*	Wadden, et al. 2013	422 (0)	35.6	46.2	6.1%	51% vs. 21%	Constipation Diarrhoea Headache	

*Patients in this study were randomized after a run-in on a low calorie diet during which mean weight loss was 6%.
BMI: body mass index; T2D: type 2 diabetes mellitus; WL: weight loss.

benzphetamine, which are rarely prescribed nowadays, and phentermine and diethylpropion, which have a very low potential to cause physical tolerance. The principal adverse effects observed in these agents are increased blood pressure and heart rate, nervousness, insomnia, dry mouth, and constipation. Phentermine may be used during alternate months since this regimen has been found to be as effective as continuous dosing[3]. The combination of lifestyle change with phentermine reduced body weight 3.6 kg, and treatment with diethylpropion in combination with lifestyle change induced a mean weight loss of 3.0 kg[50].

Orlistat was approved by the FDA in 1999 for obesity management including weight loss and weight maintenance when used in combination with reduced-calorie diet, and in 2007 it was approved as an over-the-counter medication in the USA at half the prescription dose. This agent is an inhibitor of pancreatic lipase that reduces the absorption of dietary fat by 30%. Long-term therapy with orlistat reduces overall cardiovascular risk in obese patients, with a reduction in BMI and waist circumference, reduction of hypertension, and improvement of glucose level and lipid profile[51]. One-year therapy has achieved a weight loss of 5-10%[52]. The combination of orlistat and lifestyle changes shows higher weight loss than placebo (5.8 vs. 3.0 kg; $p < 0.001$), and reduces by 37.3% the risk of developing diabetes in obese patients[53]. Orlistat is minimally absorbed from the gastrointestinal tract, and hence it has no systemic side effects.

In 2012 the FDA approved the combination phentermine/topiramate (PHEN/TPM) extended release, which contains a catecholamine releaser (phentermine) and an anticonvulsant (topiramate) approved for the treatment of epilepsy[54]. One side effect of topiramate for epilepsy resulted to be weight loss. However, the use of topiramate as an anti-obesity agent presented cognitive impairment and paresthesia as serious side effects. The combination PHEN/TPM allowed reducing the adverse events of both agents

alone by including lower doses of each agent. The EQUIP[55] and CONQUER[56] studies and the 52 extension study SEQUEL[57] were designed to assess efficacy and safety of PHEN/TPM. The EQUIP and CONQUER trial patients who received 15/92 mg dose achieved 9.4 and 8.8% more weight loss than placebo, respectively (Table 2). The SEQUEL study demonstrated that PHEN/TPM is well tolerated and effective as sustained treatment of obesity. The most common adverse effects observed were paresthesia, dry mouth, constipation, dysgeusia, and insomnia.

In 2012 the FDA also approved lorcaserin for the treatment of obesity. It is a selective 5-HT2C receptor agonist (100 times more selective than 5-HT2B receptors) that acts through the pro-opiomelanocortin system of neurons, decreasing food intake. Lorcaserin is more highly selective than fenfluramine and dexfenfluramine, two other serotonergic agents that activate the 5-HT2B receptors expressed on cardiac valvular interstitial cells. These two agents caused valvulopathy and were withdrawn by the FDA in 1997 (Table 1). The efficacy and safety of lorcaserin have been tested in three randomized trials, the BLOOM (Behavioral Modification and Lorcaserin for Overweight and Obesity Management)[58], BLOSSOM (Behavioral modification and LOrcaserin Second Study for Obesity Management)[59], and BLOOM-DM (Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus)[60] studies. These studies revealed that lorcaserin is effective for weight loss in obese patients with and without type 2 diabetes, with a mean weight loss of 5.5 kg, and headache, back pain, nasopharyngitis, and nausea as the most common adverse effects (Table 2).

Among the other agents recently used for obesity treatment there is the glucagon-like peptide 1 (GLP-1) analogue liraglutide. This agent is used for diabetes treatment, and at 2.4 and 3.0 mg doses has shown to be effective in reducing body weight in patients with type 2 diabetes. Liraglutide has also been tested to assess its efficacy in maintaining weight loss achieved with low-calorie diet. Patients treated with liraglutide together with lifestyle intervention achieved a 6% greater weight loss than the placebo group with only lifestyle intervention[61]. Moreover, liraglutide also improves insulin resistance, systolic blood pressure, glucose levels, and triglyceride concentration[62] and is well tolerated, with transient nausea and vomiting as frequent drug-related side effects (Table 2)[63].

In September 2014 the FDA approved the naltrexone hydrochloride and bupropion hydrochloride extended-release tablets as treatment option for chronic weight management in addition to a reduced-calorie diet and physical activity[64]. The naltrexone/bupropion combination is effective in the treatment of obesity, reducing placebo-subtracted weight loss of around 4.5%, with some acceptable adverse events like nausea, headache, or constipation[65].

Other drugs in development for treatment of obesity are RM-493 and beloranib. RM-493 is a melanocortin type 4 receptor agonist that targets central hypothalamic pathways, and beloranib acts on the peripheral metabolism by increasing fat oxidation[66]. There are several clinical trials in phase II to assess its efficacy and safety in obese patients, and beloranib also has one study in phase III in recruiting status[67].

Weight-loss surgery

When the methods already mentioned to lose weight have not worked, weight-loss surgery or bariatric surgery is considered if patients exhibit extreme obesity (BMI ≥ 40), obesity class 2 (BMI 35.0-39.9) and serious weight-related health problems, or when lifestyle changes are not possible. Nevertheless, bariatric surgery is associated with certain risks and complications and thus patients should be carefully selected[68].

Weight-loss surgery can follow several procedures. The malabsorptive procedure consists in shortening of the small intestine length by creating a bypass from the duodenum to a distal part of the small intestine. This shortening of the intestine reduces the time of digestion and absorption of the nutrients. Roux-en-Y gastric bypass reduces the capacity of the stomach and forms a Roux-en-Y limb-connection of this small stomach with the middle portion of the small intestine, reducing the functional length of the small intestine. Transoral gastroplasty involves passing a set of flexible staplers through the mouth into the stomach to create a restrictive pouch that limits the amount of food that can be eaten.

Bariatric surgery is a highly effective treatment in reducing body weight, and is associated with a

reduction in overall mortality. This reduction in mortality was up to 89% in nondiabetic morbidly obese patients (BMI > 50 kg/m^2) who underwent bariatric surgery[69]. Moreover, according to a meta-analysis, bariatric surgery has shown to be effective in reducing hypertension by 61.7%, resolving obstructive sleep apnea in 85.7% of patients, improving hyperlipidemia in 70% or more of patients, and completely resolving diabetes in 76.8% of patients[70].

CONCLUSION

During the last decades, the prevalence of overweight and obesity has increased to reach epidemic proportions worldwide. The Pacific Islands exhibit the highest rates of obesity, while the lowest ones have been reported in Asia. The prevalence is higher in developed than in developing countries. The increase in prevalence worldwide has been attributed to an increase of dietary fat intake and the reduction of physical activity, but there are also environmental factors and genetic predisposition to develop obesity.

A person is considered to be overweight when BMI is between 25.0 and 29.9 kg/m^2, and obese when the BMI is ≥ 30 kg/m^2.

Obesity reduces the life expectancy by two to three times, and is a risk factor for several chronic diseases such as type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, or sleep apnea. Therefore, it is considered a problem of public health and its treatment is imperative.

The treatment of overweight and obesity is based in reducing body weight. The initial goal is to achieve a weight loss of 10% from baseline. The initial treatment is based on lifestyle interventions by dietary therapy, reducing total calorie intake, increasing physical activity, and behavioral therapy to reinforce weight reduction behaviors. If lifestyle interventions are not enough to achieve the weight loss goals, pharmacologic therapy is recommended. The pharmacologic agents available mainly act by impairing dietary intake, reducing absorption of dietary fat, and increasing energy expenditure. The agents approved as anti-obesity treatment are orlistat and the sympathomimetic amines phentermine, diethylpropion, phendimetrazine, and benzphetamine. More recently, the combination phentermine/topiramate, lorcaserin, liraglutide, and the combination naltrexone/bupropion have also been approved for obesity treatment. Finally, patients with extreme obesity or obesity with serious weight-related health problems are considered for bariatric surgery, which has shown to be highly effective in reducing body weight and the risk for developing associated diseases.

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