Obesity has become a global problem, affecting countries which are developed and developing. One of the most recent and careful global estimates finds that roughly 500 million adults are obese defined as a Body Mass Index, or BMI of 30 or higher. Obesity is caused due to various factors such as environment, genetics, disease and drugs. Symptoms seen are lethargy, breathlessness, big belly, large body frame. Treatments are doing lifestyle modifications such as implementing dietary and behavioral changes. Obesity can also be controlled by changing the eating habits and doing regular exercise. Pharmacological and surgical interventions are also included in the treatment. Recently many anti-obesity drugs such as fenfluramine, dexfenfluramine, rimonabant, sibutramine, astemizole, terfinadine, phenformin, rofecoxib, valdecoxib and many others. Recently an anti-obesity drug such as belviq, qsymia has been newly introduced in the market.

The Body mass index (BMI), estimates the ideal weight of a person based on its size and weight. The Body mass index is valid for an adult man or woman (18 to 65 years). The BMI is also called index Quetelet (invented by the Belgian scientist Jacques Quetelet, 1796-1874). The World Health Organization (WHO) defines this body mass index as the standard for measure the risks associated with overweight in adults. An adult with a body mass index (BMI) greater than 30 is considered obese whereas if the BMI is 25 to 29.9 then a person is considered overweight. There can be exceptions such as, pregnant women or athletes. Their BMI could be higher but that does not mean that they are overweight. Anyone weighing more than 100 pounds is obese. A person who is overweight will not necessarily be obese. A person may appear fat but he may or may not be obese. Due to their body mechanism obese people tend to gain weight rapidly. Losing even an ounce of weight seems like a challenge for clinically obese people. Obesity has reached unprecedented levels globally and its rise is projected to continue. This has caused widespread concern, considering the associations between obesity and a range of adverse health conditions. However the picture is complicated. Overweight and obesity are major risk factors for a number of chronic diseases, including diabetes, osteoarthritis and other cardiovascular metabolic disease, while it was once an issue only in high income countries, overweight and obesity has now dramatically risen in low- and middle-income countries. Such countries are now facing a “double burden” of disease, for while they continue to deal with the problems of infectious disease and under-nutrition, they are also experiencing a rapid upsurge in chronic disease risk factors such as obesity and overweight, particularly in urban settings. Under-nutrition and obesity often exist side-by-side within the same country, the same community and even within the same household and this double burden is caused by inadequate pre-natal, infant and young child nutrition followed by exposure to high-fat, energy-dense, micronutrient-poor foods and lack of physical activity.

CAUSES

There are a variety of factors that play a role in obesity. This makes it a complex health issue to address. Behavior, environment, and genetic factors may have an effect in causing people to be overweight and obese.

Environment

People may make decisions based on their environment or community. For example, a person may choose not to walk to the store or to work because of a lack of sidewalks. Community, home, child care, school, health care, and workplace settings can all influence people's health decisions. Therefore, it is important to create environments in these locations that make it easier to engage in physical activity and eat a healthy diet.
Genetics

Science shows that genetics plays a role in obesity. Genes can directly cause obesity in disorders such as Bardet-Biedl syndrome and Prader-Willi syndrome. However, genes do not always predict future health. Genes and behavior may both be needed for a person to be overweight. In some cases, multiple genes may increase one’s susceptibility for obesity and require outside factors.

Other Factors

Diseases and Drugs

Some illnesses may lead to obesity or weight gain. These may include Cushing’s disease, and polycystic ovary syndrome. Drugs such as steroids and some antidepressants may also cause weight gain. A doctor is the best source to tell you whether illnesses, medications, or psychological factors are contributing to weight gain or making weight loss hard.

SYMPTOMS

The following are the most common symptoms that indicate an adolescent is obese. However, the patient’s appearance is sufficient to arrive at a diagnosis in most cases, determined by the person’s BMI (body mass index) depending on weight to height, though each adolescent may experience symptoms differently. Symptoms may include:

- Difficulty in doing daily activities, Large body frame.
- Lethargy, Breathlessness
- Breast region adiposity - (sagging fat cells) in boys.
- Big belly (abdomen), sometimes marked with white or purple blemishes
- Male external genitalia may appear disproportionately small
- Early arrival of puberty
- Flabby fat in the upper arms and thighs
- Knock-knees (Genu valgum) is common

The symptoms of obesity may resemble other medical problems or conditions. Psychological disturbances are also very common as well as stress, social pressure, and doing developmental chores. Always consult your adolescent’s doctor for a diagnosis.

TREATMENT

Lifestyle Modifications

The NHLBI/NAASO algorithm recommends that individuals with a BMI ≥ 30 kg/m², as well as those with a BMI of 25.0–29.9 kg/m² plus two or more disease risk factors, attempt to lose weight by adhering to a program of diet, exercise, and behavior therapy. These three components are frequently referred to as lifestyle modification and are the cornerstone of obesity treatment. Lifestyle modification is distinct from dieting. Dieting implies adhering to a particular regimen for a discrete period of time, whereas lifestyle modification involves implementing dietary and behavioral changes that can be sustained indefinitely to promote health.

Dietary Interventions

Dietary interventions for obesity are designed to create a negative energy balance (i.e., calories ingested < calories expended) by reducing daily energy intake below energy requirements. Energy requirements vary by sex, weight, and level of physical activity such that men, heavier individuals, and more active individuals have greater energy needs. Uniformly, however, greater energy deficits result in greater weight losses. Two levels of reducing diets are described below.

Low-Calorie Diets (LCDs)

An LCD is designed to create an energy deficit of 500–1,000 kcal/day and induce a weight loss of 0.5–1 kg/week. The NHLBI/NAASO guide recommends LCDs of 1,000–1,200 kcal/day for most overweight women and 1,200–1,600 kcal/day for overweight men (and for women who exercise regularly or weigh ≥75 kg). Careful self-monitoring of calorie intake is crucial to the success of LCDs. Obese individuals underestimate their intake by ~30–50%.[8] Thus, patients must be instructed in reading food labels, measuring portion sizes, and recording their food intake as soon as possible after eating. The more self-monitoring records patients complete each week, the more weight they lose.

There are several options for facilitating adherence to an LCD, including the use of structured meal plans.[9] Randomized women to one of four weight loss groups, with varying levels of structure:

1) Behavior therapy alone with a self-selected diet of conventional foods;
2) Behavior therapy plus a prescribed menu for five breakfasts and five dinners per week;
3) Behavior therapy plus the prescribed foods at a decreased price; and
4) Behavior therapy plus the prescribed foods at no cost.

Participants in groups 2, 3, and 4 lost significantly more weight after 6 months of treatment and maintained greater losses at 18 months’ follow-up than did those in group 1. This finding suggests that the provision of structure induces greater weight loss than behavior therapy alone with a self-selected diet. There were no differences in weight loss among groups 2, 3, and 4 at the end of treatment or at follow-up. This finding indicates that providing
detailed menus is sufficient to structure patients’ dietary adherence, have reported similar findings concerning the benefits of structured meal plans. Liquid meal replacements provide another method of facilitating adherence to an LCD showed that patients who replaced two meals a day with a shake lost 8% of initial weight during 3 months of treatment, whereas those who were prescribed the same number of calories (i.e., 1,200–1,500 kcal/day) but consumed a self-selected diet of conventional foods lost only 1.5% of initial weight.

**Behavior Therapy**

Behavior therapy provides patients a set of principles and techniques to facilitate their adherence to the diet and activity goals described. Common techniques include self-monitoring (of food and activity), stimulus control, slowing eating, cognitive restructuring, problem solving, and relapse prevention.

**Pharmacological Interventions**

As BMI or disease risk increase, more intensive options are available for the treatment of obesity. Pharmacotherapy is recommended for individuals with a BMI $\geq 30$ kg/m$^2$ or with a BMI $\geq 27$ kg/m$^2$ in the presence of two or more obesity-related comorbidities (e.g., coronary heart disease, type II diabetes, or sleep apnea) and who cannot lose weight satisfactorily with more conservative approaches. Two medications—Sibutramine (Meridia) and Orlistat (Xenical)—are approved by the Food and Drug Administration for the induction and maintenance of weight loss.

Sibutramine is a combined serotonin-norepinephrine reuptake inhibitor that is associated with reports of increased satiation (i.e., fullness). When used with an LCD, sibutramine (10–15 mg/day) produced a significantly greater loss of initial weight (7%) than an LCD plus placebo (2%) over the course of 1 year. Reductions of 10–15% have been observed in studies that combined sibutramine with intensive lifestyle modification. However, sibutramine is not recommended for patients with uncontrolled hypertension or a history of coronary artery disease, arrhythmias, congestive heart failure, or stroke. It is also not recommended in combination with certain antidepressant agents, such as monoamine oxidase inhibitors or selective serotonin reuptake inhibitors. Unfortunately, obese individuals are at increased risk for conditions that render the use of sibutramine inappropiate.

Orlistat is a gastric lipase inhibitor that blocks the absorption of about one-third of the fat contained in a meal, leading to the loss of about 150–180 kcal/day. The greatest benefit of pharmacotherapy may reside in facilitating the maintenance, rather than the induction, of weight loss.

**Surgical Interventions**

Bariatric surgery, the most intensive treatment for obesity, is appropriate only for those individuals with a BMI $\geq 40$ kg/m$^2$ or BMI $\geq 35$ kg/m$^2$ in the presence of comorbidities. Typically, people who seek bariatric surgery have exhausted the more conservative weight loss options without satisfactory results.

The two most common surgical procedures for obesity are vertical banded gastroplasty (VBG) and gastric bypass (GB). Both entail isolating a small (15- to 30-ml) pouch of stomach with a line of staples, thereby drastically limiting food intake. In VBG, the pouch empties into the remaining stomach, where the digestive process continues as normal. GB, however, not only restricts food intake, but also reduces absorption by bypassing the remaining stomach and 45–150 cm of small intestine.

Bariatric surgery produces average reductions of 25% (VBG) to 30% (GB) of initial weight and significant improvements in hypertension, asthma, sleep apnea, and diabetes. Improvements in mood have also been reported, but they appear to wane with time. These findings undoubtedly have contributed to the recent surge in popularity of bariatric surgery, as has the ability to perform the procedures laparoscopically. Laparoscopy reduces hospital stay time, as well as operative morbidity and mortality.

**DISEASES CAUSED BY OBESITY**

Research has shown that as weight increases to reach the levels referred to as "overweight" and "obesity," the risks for the following conditions also increase:

- Coronary heart disease
- Type 2 diabetes
- Cancers (endometrial, breast, and colon)
- Hypertension (high blood pressure)
- Dyslipidemia (for example, high total cholesterol or high levels of triglycerides)
- Stroke
- Liver and Gallbladder disease
- Sleep apnea and respiratory problems
- Osteoarthritis (a degeneration of cartilage and its underlying bone within a joint)
- Gynecological problems (abnormal menses, infertility).
DRUGS BANNED IN INDIA FOR ANTI OBESITY

1. Fenfluramine and dexfenfluramine

Fenfluramine and dexfenfluramine were used to treat obesity. They were widely used in slimming centers. However, they were withdrawn due to reports of diseases of heart valves, fibrosis of the heart and pulmonary hypertension. The combination of fenfluramine and phenteramine, another weight loss pill was particularly notorious for causing heart valve problems and sudden death.

2. Rimonabant

Rimonabant was particularly effective in causing weight loss. It inhibited the action of substances called cannabinoids in the brain. It has been withdrawn due to serious side effects like depression, suicidal tendencies and seizures.

3. Sibutramine

Sibutramine is a weight loss pill that has been recently banned since it caused heart related side effects.

4. Astemizole and terfenadine

Astemizole and terfenadine are antihistamines that were used to treat allergies. They were banned since they could cause a heart condition called polymorphic ventricular tachycardia and even death when used in high doses or with drugs like erythromycin, clarithromycin and ketoconazole.

5. Phenformin

Phenformin is an antidiabetic drug similar to metformin. It has been banned since it carries a high risk of lactic acidosis.

6. Rofecoxib and valdecoxib

Rofecoxib and valdecoxib were popular painkillers that were used for arthritis and other painful conditions. They resulted in pain relief without causing gastric side effects. However, they were withdrawn due to concerns of heart attack and stroke with their use.

7. Rosiglitazone

Rosiglitazone is a drug used in the treatment of type 2 diabetes. It has been banned due to an increased risk of heart attacks.

8. Gatifloxacin

Gatifloxacin is an antibiotic whose use as an oral and injectable drug has been recently banned in India. This is due to its risk for severe hyperglycemia or high blood sugar levels in the elderly.

9. Tegaserod

Tegaserod is a drug that is used to treat patients with irritable bowel syndrome with predominantly constipation. It was withdrawn from the market since patients taking this drug showed increased incidence of heart attack and stroke.

RECENT DRUGS/TREATMENT USED FOR ANTI OBESITY

A new, FDA-approved weight loss drug hit the market. It’s called Belviq. It’s prescription only because it’s designed for those who are obese or significantly overweight. John Grohol, PsyD, a psychiatrist and the founder and CEO of Psych Central writes: “Belviq appears to work by turning on a specific chemical switch in the brain that increases levels of serotonin. It’s not clear exactly why this helps a person lose weight.” Belviq is available with a prescription for patients who are obese - defined as having a body mass index (BMI) over 30 -- or for certain overweight patients who are not obese but have a significant health problem like diabetes, high blood pressure, or high cholesterol. Like all drugs, Belviq has certain side effects. Women who are pregnant or nursing shouldn’t take it due to the risk serotonin syndrome -- a dangerous chemical imbalance. It can also pose problems for people taking certain medications for heart disease, depression, migraine or anxiety disorders. The FDA recommends patients stop taking Belviq after three months if they fail to lose five percent of their body weight. Another anti-obesity prescription drug, Qsymia, also went on the market recently but in limited supply. It’s expected to become more widely available this year.

Table 1 Promising Drugs For The Treatment Of Obesity

<table>
<thead>
<tr>
<th>Phase III drugs</th>
<th>Phase II drugs</th>
<th>Phase I drugs</th>
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<tbody>
<tr>
<td>Empatic (zonisamide + bupropion)</td>
<td>Antiepileptic dopamine and noradrenaline reuptake inhibitor</td>
<td>TPN435 AgRP (agouti-related protein) inhibitor</td>
</tr>
<tr>
<td>Pramlintide/metreleptin</td>
<td>Leptin analog + amylin analog</td>
<td>ZGN-433 D3 (dopamine) antagonist</td>
</tr>
<tr>
<td>Liraglutide Long</td>
<td>Pancreatic lipase inhibitor</td>
<td>PP1420 Pancreatic polypeptide analog</td>
</tr>
<tr>
<td>Tesofensine</td>
<td>Neuropeptide Y5 receptor antagonist</td>
<td>GSK598809 D3 (dopamine) antagonist</td>
</tr>
<tr>
<td>Velneperit</td>
<td>PYY3-36 and pancreatic polypeptide analog</td>
<td>AZD 7687 DGAT1 (diglyceride acyltransferase) inhibitor</td>
</tr>
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</table>

PREVENTION

Many of the strategies that produce successful weight loss and maintenance will help prevent obesity. Improving your eating habits and increasing physical activity play a vital role in preventing obesity. Things you can do include:
Eat five to six servings of fruits and vegetables daily. A vegetable serving is one cup of raw vegetables or one-half cup of cooked vegetables or vegetable juice. A fruit serving is one piece of small to medium fresh fruit, one-half cup of canned or fresh fruit or fruit juice, or one-fourth cup of dried fruit.

Choose whole grain foods such as brown rice and whole wheat bread. Avoid highly processed foods made with refined white sugar, flour and saturated fat.

Weigh and measure food to gain an understanding of portion sizes. For example, a three-ounce serving of meat is the size of a deck of cards. Avoid super-sized menu items particularly at fast-food restaurants. You can achieve a lot just with proper choices in serving sizes.

Balance the food “checkbook.” Eating more calories than you burn for energy will lead to weight gain.

Weigh yourself regularly.

Avoid foods that are high in “energy density” or that have a lot of calories in a small amount of food. For example, a large cheeseburger and a large order of fries may have almost 1,000 calories and 30 or more grams of fat. By ordering a grilled chicken sandwich or a plain hamburger and a small salad with low-fat dressing, you can avoid hundreds of calories and eliminate much of the fat intake. For dessert, have fruit or a piece of angel food cake rather than the “death by chocolate” special or three pieces of cheesecake, you can avoid hundreds of calories and eliminate much of the fat intake. For dessert, have fruit or a piece of angel food cake rather than the “death by chocolate” special or three pieces of cheesecake

CONCLUSION

There is a huge problem in the current pharmacological treatment options for obesity. Obesity has been identified as the second most factors contributing to preventable death. Many factors have mitigated against active drug development, including the poor safety and efficacy of previous anti-obesity drugs. The new generation of anti-obesity drugs offers hope for the management of obesity, although no single agent is likely to be a remedy. The prescribed drugs have some or the other side effects. If sustained success is to be achieved, obesity will need to be managed like many other chronic diseases with combination therapies and long-term treatment. Lifestyle modifications, pharmacological interventions and surgical interventions, behavior therapy are some of the treatments for obesity.

REFERENCES:


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