

Treatment of Obesity

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The most commonly used methods specified by the World Health Organization (WHO) for exhibiting, classifying and determining the type of the obesity that is defined as excessive fat accumulation in the body are body mass index (BMI) and measuring waist circumference. BMI is measured by dividing the body weight in kilograms by the height in meters squared and its unit is kg/m². The BMI is classified as slim if BMI is smaller than 18.5 kg/m²; normal if BMI is in between 18.5-25 kg/m² and pre-obese if BMI is in between 25-30 kg/m². If BMI is greater than 30 kg/m², it shows obesity and it is divided into three classes; stage I (BMI 30-40), stage II (BMI 40-50) and stage III (BMI>50). The pear-type obesity (female type obesity) is formed by the accumulation of fat especially in the hip region and it does not show close relationship with obesity related diseases. The apple-type obesity (male type obesity) means the fat accumulated in the waist region and is more prone for the diseases. Waist circumference that is greater than 94 cm in men and 80 cm in women is associated with cardiovascular disease.

The treatment of obesity should be continued lifelong like other chronic diseases (hypertension, hyperlipidemia, diabetes mellitus etc.) The treatment seems easy theoretically but in practice it is really hard to manage. Obesity is a serious risk factor for a large amount of diseases like coronary heart disease, hypertension, stroke, type 2 diabetes, cancer (endometrium, breast, prostate and colon), osteoarthritis, varicose, sleep apnea syndrome, ovarian cysts and depression.

Factors that Affect Development of Obesity

Age, sex and ethnicity are the demographic factors that take role in obesity. Obesity is frequent in women and increases with age. With the decreasing level of income and education, obesity rates are increasing in developed countries. The number of births a person has undergone increases the amount of weight they gain. Fast food consumption significantly increases obesity. Quitting smoking, alcohol consumption and inadequate physical activity (exercise) are also related with gaining weight.

Some drugs can take role in the etiology of obesity. Glucocorticoids, insulin, sulfonylurea, antidepressants, antihypertensive drugs, progesterone, phenothiazine, cyproheptadine and lithium can be considered among these drugs.

Obesity Treatment

Over 95 percent of patients who are under obesity treatment and lose weight put on weight again; so just as losing weight is important, maintaining that weight is also essential. Obesity treatment includes various types of methods like diet, exercise, behavioral therapy, medical therapy, combined therapy and surgical therapy.

Even a 10 percent of decrease in the body mass helps reduce the risks of diseases caused by obesity. Because of that, the actual treatment suggestions target that ratio and their aim is to provide long term maintenance for weight loss. The main point in the treatment must be consuming more energy

than obtaining it. The treatment is adequate in patients that have BMI values in between 25.0 – 29.9 kg/m² and two or more risk factors (hypertension, diabetes and dyslipidemia). If the patient has a BMI of 30 kg/m² or more, the treatment must be applied regardless of risk factors.

Diet Therapy

The diet in obesity treatment is personalized and it is planned according to age, sex, habits, biochemical markers, the degree of obesity and any accompanying diseases. The trait of this diet is that it has a low calorie level that provides the patient with less energy intake than he/she consumes. The purpose of the diet therapy is to provide a reduction in the fat storage of the body by causing energy deficiency. Daily calorie intake should be separated into meals, such as 20-25 percent for breakfast, 30-35 percent for lunch and 30-35 percent for dinner. Before diet therapy, personal daily calorie need must be estimated.

Exercise

In obesity treatment, the exercise gives optimum results and when it is combined with reduction of energy intake, it provides more weight loss compared to only diet and it also protects the muscles. 3-5 days per week and 30-45 minutes per day of moderate level physical activity should be recommended. Before beginning of the exercise program, cardiovascular and respiratory system checks should be made. The exercises that increase energy consumption and have minimal risk should be chosen. Exercise program must be long and moderate level as in the walking. The mean calorie consumption should be approximately 300 calories per day and totally 1000 to 2000 calories for a week. Body mass must reduce maximum 1 kg for a week.

Behavioral Therapy

It will be reasonably functional that if behavioral therapy is added to diet and physical activity. Implementation of routine behavioral strategies for facilitating diet and exercise is extremely important in losing weight and making the weight stable. Self-monitoring, stress management, stimulus control, problem solving, probability management, cognitive restructuring and social support can be exemplified among the behavioral approaches declared as useful. In self-monitoring; calorie intake, exercises and behaviors like drug usage and body weight changes should be monitored and kept by the patient. In stimulus control; with the help of the records that patient kept, to determine and control the factors that stimulate bad eating habits like eating while watching TV are asked from the patient.

Medical Treatment

The medicine used for losing weight and certified by FDA (US

Food and Drug Administration) can be added the therapy program for the patients that have BMI value equal or greater than 30 kg/m². Medical treatment should be applied with behavioral therapy, diet and exercise or various combinations of them. Nowadays, the medicine used to treat obesity can be summarized like that;

Appetite Suppressant Agents

The most frequently recommended drugs in the obesity treatment are the drugs that suppress the appetite.

Sibutramine

Sibutramine inhibits norepinephrine and serotonin reuptake in central nervous system and so reduces to desire to eat. It is the single drug that is accepted for long term usage but in the other hand, because of its cardiovascular side effects, it was picked off and got out of use in the beginning of the 2010.

Rimonabant

The endocannabinoid system is a neuronal regulatory system that provides to control food intake and it considerably attracts attention in these days. Rimonabant is cannabinoid receptor blocker and developed against to CB1. Weight loss with rimonabant has exhibited through various studies. Topiramate

Topiramate that used to treat epilepsy and migraine is also an anti-obesity drug and its efficiency and safety have shown on clinical studies [1-3]. It has significant side effects like paresthesia, difficulty in concentration, somnolence and metabolic acidosis. It is not chosen as standalone agent for obesity treatment. It can be used with the combination of phentermine.

Zonisamid

It is an antiepileptic drug that inhibits sodium and calcium channels and also has serotonergic and dopaminergic activity. It has gastrointestinal, central nervous system and psychiatric side effects. It is not recommended in obesity treatment.

Fat Absorption Inhibitors

Orlistat

Orlistat is recommended for the first step pharmacological treatment of obese patients because of its cardiovascular safety profile and favorable effects on LDL and cholesterol levels. The treatment guidelines suggest orlistat treatment up to 2 years. Orlistat inhibits pancreatic lipase in the bowel and so prevents absorption of approximately one third of the fat that obtained in small bowel. The most important side effect is intestinal loss or fat loss with feces.

Lorcaserin

It is an alternative drug for the patients cannot tolerate orlistat. If the patient does not lose 5 percent of his/her weight in 12 weeks, lorcaserin must be stopped because long term safety data is limited.

Combination drugs

Because of regulation of food intake is controlled with different ways, the hypothesis purposed that making drug combinations with the drugs have different mechanism of action is more efficient when it is compared with single drug therapy.

Phentermine - Topiramate

In 2012, usage of phentermine and extended-release topiramate combinations is validated by FDA for the patients that have the BMI value over 30 kg/m² or over 27 kg/m² but if there is accompanying at least one of the co-morbid conditions like hypertension, diabetes and dyslipidemia. The most common side effects are paresthesia, constipation and dry mouth [4,5]. There is a dose dependent increase in the side effects like depression, anxiety and attention deficit. A rise in the heart rate and blood pressure is determined. The drug is contraindicated in pregnancy because orofacial clefts were seen in the babies exposed to the drug in first trimester. Pregnancy test must be made to women of childbearing age before beginning of the drug and monthly after usage. Also it is contraindicated for the patients have hyperthyroid, glaucoma and take monoamine oxidase inhibitors in last 14 days. Topiramate can cause kidney stones, so this combination should be used carefully in the patients have the history of kidney stones. This combination is also not recommended for the patients have cardiovascular diseases (hypertension or coronary heart disease). Phentermine- topiramate can be chosen for the obese men and premenopausal women that do not have cardiovascular disease and cannot tolerate orlistat and lorcaserin. If a patient cannot lose 5 percent of his body weight in 12 weeks even with maximal dose, phentermine- topiramate combination should be stopped slowly.

Bupropion - Naltrexone

Headache, constipation and nausea are the most common side effects. This combination does not exist commercially.

Anti-Diabetic Medication

Metformin

It is a biguanide that certificated for DM and obesity [6].

Pramlintide

Pramlintide is an analog of amylin that known as islet amyloid

polypeptide. Amylin is a peptide hormone that releases from pancreatic beta cells with insulin as an answer to the food intake. It slows gastric emptying and reduces food intake. Unlike the other anti-diabetic medicines and insulin; Pramlintide is associated with moderate level weight loss [7,8].

Exenatide

Exenatides are also named incretin peptides (glucagon like polypeptide-1 [GLP- 1]) and glucose dependent insulinotropic polypeptide (GIP). They are gastrointestinal peptides that stimulate insulin release depending on glucose. GLP-1 also prevents glucagon discharge and stomach emptying. Exenatide is a long-acting oral GLP-1 receptor agonist and it can be used as an additional treatment for the patients with type 2 diabetes mellitus which is regulated by oral anti-diabetics. The drug is administered as subcutaneous injections twice a day.

Liraglutide

Liraglutide is a long-acting analog of GLP-1. The drug is applied under the skin once a day. The studies which compare placebo or glimepirid with liraglutide show an important weight loss (2,0-2,5 kg) in the patients who use liraglutide [9]. Side effects like nausea and vomiting are seen in most of the patients that use liraglutide and weight loss can be a result of these side effects.

Thermogenic Agents

Thyroid Hormone

Thyroid hormone is not effective in obesity treatment, although it has catabolic effects. Thyroid replacement therapy is contraindicated in energy restricted diets.

Sympathomimetic Agents

Sympathetic nervous system suppresses food intake and increases energy consumption. Adrenergic agonists are still used to treat obesity but they should be considered very carefully like amphetamines. Their addictive potential and the possibility of abuse cannot be ignored. When the treatment is over, the patient gains weight again and side effects can be seen like hypertension, diabetes and worsening of coronary insufficiency.

The metabolic studies have demonstrated that the thermogenic effect of nicotine which is the active material of cigarette. Pharmacological studies have shown that the thermogenic effect of nicotine is due to release of adrenal catecholamines into the blood.

Other addictive drug that has sympathomimetic and significant weight loss effects is cocaine. The chronic use of cocaine by inhaling always leads to weight loss.

In the long term pharmacotherapy for weight loss, sympathomimetic drug (phentermine, diethylpropion, and phendimetrazine, benzphetamine) use is not recommended because of their probability of abuse.

Experimental Drugs

Leptin

Leptin is a peptide produced in adipose tissue. Leptin is an anti-obesity factor. It reduces food intake and causes losing weight by activating sympathetic nervous system [10].

Serum leptin levels increase depending on leptin resistance in obese adults.

Peptide YY (PYY)

This is a bowel hormone that suppresses appetite and reduces food intake. Common side effects are nausea and vomiting. Oxyntomodulin is a product of proglucagon gene. It is produced in the L-cells that belong to the gastrointestinal tract. It plays a role in suppression of appetite.

Melanocortin-4 Receptor Agonists

Hypothalamic melanocortin system plays an important role in the control of body weight.

Nutrient Separator Agents

Androgens

Androgen implementation leads to nitrogen retention and an energy increase in lean tissue including muscle tissue. Energy expenditure increases with increase in the amount of lean tissue.

Growth Hormone

Growth hormone implementation to adults in pharmacological doses stimulates lipolysis and lipid oxidation and reduces body fat stores. The agent has prevented widespread use to treat obesity until today, because of the expensiveness of recombinant growth hormone and adversely affecting insulin resistance and hypertriglyceridemia.

Dietary Supplements

There is limited evidence to support the efficiency and safety of dietary supplements. Samples of dietary supplements are ephedra, green tea, chromium, chitosan, and guar gum. The guar gum derived from the Indian cluster bean due to an increased viscosity of the contents of the stomach leads to a feeling of postprandial satiety. Adverse effects of guar gum have been reported as stomachache, abdominal bloating, and diarrhea in meta-analysis of studies [11]. In the meta-analysis of studies with green

tea in overweight or obese adults, it was observed that green tea causes significant weight loss [12]. Clinicians should be careful about usage of weight loss formulations and patients which prefer to use these supplements should be monitored.

Calcium

Epidemiological data has shown the significant effects of calcium supplementation on body fat or weight loss [13,14].

Surgical Treatment

According to NIH co-decision, surgical treatment is a candidate for the severe obese patients (BMI > 40 kg/m²) when the diet, exercise, and drug therapy have failed and the obese patients that have high rates of morbidity and mortality (hypertension, diabetes, dyslipidemia, sleep apnea, and impaired glucose tolerance) even if BMI value is in between 35-40 kg/m². In addition, this treatment can be assessed when other methods fail.

The surgical methods for treating obesity are listed below;

- Gastric resection
- Horizontal gastroplasty
- Vertical banded gastroplasty
- Gastric banding
- The methods that make malabsorption
- Jejunioileal bypass
- Retrocolic loop bypass
- Roux-en Y gastric bypass
- Combinations
- Laparoscopic anti-obesity surgery
- Biliopancreatic diversion
- Liposuction
- Lipectomy

An adjustable gastric band is placed in the upper portion of the stomach in adjustable gastric banding, it is also known as stomach staple method. Band progressively compressed to create a small pouch.

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