

# CLINICAL AND THERAPEUTIC ASPECTS OF OBESITY

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**Abstract:** Obesity is best defined as the presence of an abnormal absolute amount or relative proportion of body fat. The most serious medical conditions associated to obesity are type 2 diabetes mellitus, hypertension, coronary artery disease, respiratory disease, gallbladder disease, osteoarthritis and cancer. The treatment of obesity has three important aspects: changing the lifestyle (diet, physical exercises), pharmacologic therapy and surgical treatment.

**Keywords:** obesity, medical conditions associated to obesity, treatment

**Rezumat:** Obezitatea este cel mai bine definită ca prezența unei proporții absolute sau relative anormale de țesut adipos. Cele mai serioase afecțiuni asociate obezității sunt diabetul zaharat de tip 2, hipertensiunea arterială, boala coronară ischemică, boala respiratorie, afecțiunile vezicii biliare, osteoartrita și cancerul. Tratamentul obezității cuprinde trei aspecte importante: modificarea stilului de viață (dietă, activitate fizică), farmacoterapia și tratamentul chirurgical.

**Cuvinte cheie:** obezitate, afecțiuni asociate obezității, tratament

lipolysis and that vary according to the distribution of the adipose tissue. In both genders, the lipolytic response to adrenaline is higher in the abdominal adipose tissue than the gluteal or femoral response. Cortisone may contribute to this increase of lipolysis, by inhibiting the anti-lipolytic effect of insulin. These factors stimulate an excessive release of free fatty acids from the abdominal adipocytes in the port system. The increase of the free fatty acids (FFA), especially post-prandially, when it is usually suppressed by insulin, will lead to the improper maintenance of the glucose production and to the alteration of the hepatic use of glucose.

The decrease of the insulin hepatic clearance leads to the increase of the insulin peripheral concentration and to the decrease of the regulation capacity of the insulin receptors. In the initial stage, the pancreas may respond by maintaining a compensatory hyperinsulinemia status, the decompensation of the glucose tolerance being prevented. With each increase of the plasmatic concentration of the FFA, the patients are no longer able to continue and to maintain the compensatory hyperinsulinemia condition, resulting hyperglycemia.

Hyperinsulinemia and insulin resistance is correlated to the dyslipoproteinemic status and may contribute to the characteristic alteration of the lipidic plasmatic profile associated to obesity, to the increase of the plasmatic concentration of triglycerides, HDL-cholesterol decrease, to the increase of the total cholesterol and of the LDL cholesterol.

X syndrome is characterized by abdominal obesity, hypertriglyceridemia, reduced HDL cholesterol, hyperinsulinemia, glucose-intolerance and hypertension. The total blood volume is high in obesity, being proportional with a ponderal increase. Obesity increases the cardiovascular risk, hypertension and the coronary arterial disease.

Fibrinogen is an important predictor of the coronary arterial disease and of the future cardiovascular events and may play a direct part in the atherosclerotic processes. Fibrinogen stimulates the proliferation of the smooth muscles; it is a component part of the atheroma plate, initiates the platelet aggregation and contributes to the blood viscosity. Obesity leads to the alteration of the respiratory system, to the reduction of the pulmonary

Obesity represents a medical and social problem reaching endemic proportions at international level, characterized by the excessive accumulation of adipose tissue. Most of the times, this is determined by the association of the genetic component of the external factors, such as an unhealthy lifestyle due to hypercaloric foodstuffs, sedentary life and alcohol consumption. Obesity complications depend on the size of the adipose tissue and on its topography. The most important affections associated to obesity are: type 2 diabetes mellitus, hypertension, respiratory diseases, coronary arterial disease, gallbladder disease, osteoarthritis and cancer. The metabolic syndrome may be considered as one of the most important comorbidities of obesity.

The factors that contribute to the occurrence of the diabetes mellitus in the obese patients are the increase of the insulin quantity, insulin-resistance increase, the decrease of the glucose transportation stimulated by insulin in muscles and adipocytes.

The different deposits of the adipose tissue have a different response to the hormones that regulate

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volume and to the alteration of the ventilation pattern. A decrease of the libido and impotence may occur in the obese people and regarding the obese women, an increase of the incidence of the functional uterine bleedings and amenorrhea.

In the obese men, testosterone concentration is reduced; it is an inverse relation between the plasmatic testosterone and the body mass. In the obese women, the plasmatic testosterone and androstenedione are increased, the relation estrone/estradiol is reduced – a pattern similar to the polycystic ovary syndrome, while in the female patients with simple obesity, the LH and FSH response to the LHRH stimulation is normal, as well as the release of gonadotropes after the administration of clomiphene.

In the obese female patients, the loss of weight brings about reversible biochemical changes and the occurrences of menses.

Hepatic steatosis is frequent in the obese patients, especially in those with central distribution. The reason is due to the oxidative stress and lipidic peroxidation, factors associated to a normal production of cytokines, FFA increase and insulin-resistance.

Biliary lithiasis is also frequent in obesity, because of a solubility deficiency that leads to an oversaturation of the bile, possible due to the hepatic secretion of the cholesterol in the bile.

The most frequent cancer forms associated to obesity are the colorectal and prostate cancer in men and breast, urinary bladder cancer in women. The adipose tissue contains increased levels of aromatase, an enzyme that transforms the androgens in estrogens. The estrogens serve as increasing factors in the breast and endometrial cancer. At the same time, due to the increase of the biomechanical forces, directed towards the articular surfaces, osteoarthritis also occurs in obesity.

Other complications that may occur in obesity are represented by the gastro-oesophageal reflux, secondarily to the hiatal hernia, intertrigo, edema of the lower limbs, venous insufficiency, excessive sweating, hyperuricemia, psychological and psychiatric problems.

When assessing an obese patient, special attention must be paid to the patient's medical history, risk factors, complications, minimum and maximum weight, the moment when the patient has put on weight, diet history, family history regarding obesity, food customs, physical activity, lifestyle, alcohol consumption, smoking, relevant social history, drugs associated to the weight increase, stress factors. The clinical examination should establish the height, weight, the body mass index (BMI), waist and hips circumference, arterial hypertension, presence of the coronary disease, pulmonary hypertension, cor pulmonale, congestive cardiac insufficiency, optic fundus examination. From the endocrine point of view, it is necessary to appreciate the signs of hypothyroidism; dry teguments, frilosity, sleepiness, memory decrease, slow intestinal transit, round face, linear atrophy, menses disorders.

Laboratory investigations should contain the determination of glycaemia, lipidic profile, presence of

glucose and protein in urine, hormones dosages: T3, T4, TSH, free urinary cortisol, 17 hydroxycorticosteroids, estradiol, FSH, LH, prolactin, plasmatic testosterone.

Obesity treatment long term objectives are the loss of weight and the decrease of the risk factors. Following the loss of weight, it is important to maintain the new weight and to prevent the patient to gain weight again.

Obesity treatment comprises three important aspects: changing the lifestyle, pharmacotherapy and the surgical approach. Changing the lifestyle suggests changes in diet, physical activity and in food customs. A low caloric diet (800-1200 kcal/day) is recommended as against a very low caloric diet (below 800 kcal/day). The reduced caloric diet may decrease the weight on average, bringing about a reduction of the adipose tissue after a period of almost 6 months.

The physical activity, 3-7 sessions / week, each of 30-60 minutes, may determine a reduction of weight with 2-3%. The behavioural therapy aims at changing the food customs by the identification of the food stimuli, self-assessment and supportive groups. Associating a low caloric diet to the physical activity and to the behavioural therapy proved to give better results, as against the independent diet or physical activity.

Pharmacotherapy is recommended when the lifestyle changes are inefficient. Pharmacotherapy is considered necessary when the body mass index is higher than 30 kg/m<sup>2</sup>, or if there is any comorbidity. For a drug to be efficient in the treatment of obesity, it should meet two criteria: the average loss of weight on year after, should be at least 5% higher than in the control group, and the number of patients who receive drugs and who loose at least 5% of weight one year after, should be higher than the control group.

In order to loose weight, Orlistat and Sibutramine are the most frequently used.

Orlistat is an inhibitor of the pancreatic and gastro-intestinal lithiasis, preventing the absorption of at least 30% of the food fats, induces the decrease of cholesterol and of the LDL cholesterol, independently of the weight loss.

Sibutramine induces the weight loss by inhibiting the recollection of norepinephrine and serotonin and by the sympathetically mediated thermogenesis.

These drugs bring about a loss of weight of 6-10% of the initial weight one year after, and a significant gain in weight immediately after the interruption of the medication.

Leptin, whose concentration is high in obesity, was administered in large doses, with reactions at the level of the injection place. It has been used a form of leptin with long term action, which determined a decrease of weight in comparison with the placebo group. It is a medication of research and of the future.

Other possible future therapeutic agents: ciliary neurotrophic factor (CNTF), endocannabinoids, antagonists NPY, antagonists of the MC4R receptor, inhibitor of protein-thyroxine phosphatase-1 b, intranasal

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administration of PYY – an antagonist of GH-relin, oxyntomodulin, a long acting agonist for GLP1, an agonist of CCK, GIP (gastric inhibitory polypeptide), adiponectin. Obesity surgical treatment should be reserved to the patients with a body mass index higher than 40 or BMI > 35 with associated comorbidities. The surgical treatment should be taken into consideration after the failure of the conventional therapy of obesity: changes in diet and food customs, physical activity and pharmacotherapy. Weight loss planning should be in stages: periods of time for a balanced weight loss of 0,5-1kg per week, lasting for 1-3 months through diet, physical activity, medication and behavioural therapy, periods of time of 2-4 months for preserving the new weight, through a diet with classical moderate caloric supplement and with the increase of the physical activity and of the behavioural therapy.

In conclusion, the treatment efficiency will be assessed through a loss of weight of 0,5-1 kg per week, through the improvement of the associated conditions and of the life quality in order to reach a normal BMI.

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