Trearment of metabolic syndrom

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Treatment of metabolic syndrom: *. It is necessary to diagnose correctly the Metabolic syndrome. Treatment of metabolic syndrome is carried out on the basis of obesity, AH (arterial hypertension), hyperlipidemia, pancreatic/insular diabetes, taken into consideration. The leading meaning for the obesity treatment has the balanced meal or adequate diet. Criteria. The adequate dietary cure and medical therapy of metabolic syndrome are proposed in this work. The surgical methods for the treatment of obesity are also learnt.*

Key words: *Methabolic syndrome*, *Diet, Dietotherapy, Medication, Obesity, Body Weight Regulation, Sibutramine, Orlistate.*

INTRODUCTION

Treatment of metabolic syndrome is carried out on the basis of taking into consideration all components, which metabolic syndrome (obesity, AH (arterial hypertension), hyperlipidemia, pancreatic/insular diabetes) are expressed by.

Treatment of obesity is integrated. The leading significance has the balanced meal or adequate diet. The main goal of obesity treatment is the body weight loss and its maintenance on the defined level. The initial aim of dietotherapy is 5-15% reduction of a body weight during the period of six month. Reduction of a body weight to the ideal mass is very important stimulus for patient, but it is usually very difficult to achieve it.

On the basis of US Institute of Health Care (1999) data - after body weight reduction in 60% of cases its restoration occurs in one year, another cases – in 5 years.

Keeping a normal weight is a constant battle. They gain back the weight that they loose the minute they go off their diet. After many years of this *back and forth*, clinical complications arise. Relapses are very common, despite patients' continuous efforts to keep the weight off.

GENERAL REGULATIONS OF DIETOTHERAPY

0.5 kg reduction of body weight during a week – is “well”, 1,0 kg – is “perfect”, but more than 1,0 kg - is “potentially dangerous”. 5-15 % of the body weight loss reduces the cardiovascular system diseases at 8%, insular diabetes – 44%, total mortality - 20 %, mortality due to cancer - 37 % .

At the beginning of dietotherapy the physical condition of patient is estimated during 1-2 week in according to the patient’s dairy, what makes it possible to do the analysis of dietary habits, ration and intaken food quantity.

It was cleared up, that in the patients with obesity is noted a large amount of consumable fats (150 g per day/twenty-four hours, i. e. 50-60% of energetic value of ration), which makes on the average the high enough daily caloric value of food >3300 kcal. The dietary habits disturbance is noted: infrequent taking the food (2 times a day), ignoring the breakfast, late supper.

The individual food allowance/ration have to be planned with taking into account the following principles:

1) reduced calorie content;

2) limited amount of fats, carbohydrates and alcohol;

3) increasing the amount of low-calorie food taking with significant content of plant/vegetable fibers;

4) balancing of proteins, vitamins and minerals;

5) repeated nutrition (5-6- meals a day)

6) taking the food mainly at the first half of day ;

7) the fasting days are required;

8) it is necessary to regulate the caloricity of food agreeably to time of day:

- ✓ breakfast – 20 % of total caloricity;
- ✓ second breakfast /lunch– 10 %;
- ✓ dinner – 35-40 %;
- ✓ afternoon snack – 10-15 %;
- ✓ supper – 15-20 %.

Last mealtime - 19:00.

Very low-calorie diet may stimulate the development of steatohepatosis, cholelithiasis, undernourishment syndrome.

The fasting days are often done for the dietotherapy efficiency encreasing: 700-900 kcal in five steps meal a day (1-2 times a week). The fasting days with apples (1,5 kg), watermelon, vegetables (1-2 kg of salad), gottage cheese (300-400 g), potatoes (1-1,5 kg, baked in their jackets) and the protein fasting days (gottage cheese, meat) are much more easier taken for patient, than vegetable diet.

The patient with obesity have to know that, in spite of the low-calorie diet, the moment, when body weight "freezes" on the certain level, may coming up during the body weight reduction. It may be cause by limitation of general level of metabolism, therefore it is necessary to intensify the physical activity – effective aerobics, running, swimming, skiing, walking.

A NATURAL TENDENCY TO RETAIN THE WEIGHT

A common affliction is that the weight increases with a near normal or a greater than normal intake of. This common clinical complaint, scientifically ignored for many years, has now been accepted as the main cause for the difficulty obese people experience in maintaining a desirable weight after continuous dieting (set-point of body weight control).

Even when their intake of food is the same a normal weight these patients have a tendency to gain weight well beyond what would be expected for the number of calories consumed. They keep their set-point of body weight control at a higher level than what it should be according to their age, sex, or height.

THE HEALTH RISK OF BEING OVERWEIGHT

Obesity is not just a matter of being overweight. It is also hazardous to health. Although some near-normal weight subjects also may suffer the same clinical complications as obese individuals, such as hypertension, gout and the non-insulin dependent type of diabetes

On the other hand, despite an increased accumulation of adipose tissue, some moderately overweight subjects do not show the classical complications of obesity. This is particularly true of females. For these patients, just reducing body weight is enough to improve their clinical condition.

There are some diseases that are often associated with obesity. The most important of these disorders that obesity appears to play a role in precipitating or at least aggravating are: The stable type of diabetes (now called NIDDM), non-insulin dependent diabetes mellitus, gout, rheumatism, arthritis, high blood pressure and atherosclerosis, coronary disease, cerebral hemorrhage and cancer.

MEDICATION OR PHARMACOTHERAPY

Classification of medical preparation

I group – preparations to limit the meal –antiobesity drugs: sibutramine, fentermine, fenfluramine,deksfenfluramine;

II group – preparations to intensify the consumption of energy: cibutraine, termogenic sympathomimetics;

III group – preparations to reduce the intake of nutrients/intestinal absorption – orlistat.

Sibutramine (trade name Meridia in the U.S. and Canada, Reductil in Europe and most other countries), usually as sibutramine hydrochloride monohydrate, is an orally administered agent for the treatment of obesity, as an appetite suppressant. It is a centrally-acting serotonin-norepinephrine reuptake inhibitor structurally related to amphetamines, although its mechanism of action is distinct.

Pharmacokinetics

Sibutramine is well absorbed from the gastro-intestinal (GI) tract (77%), but undergoes considerable first-pass metabolism, reducing its bioavailability. The drug itself reaches its peak plasma level after 1 hour and has also a half-life of 1 hour. Sibutramine is metabolized by cytochrome P450 isozyme CYP3A4 into two pharmacologically-active primary and secondary amines (called active metabolites 1 and 2) with half-lives of 14 and 16 hours, respectively. Peak plasma concentrations of active metabolites 1 and 2 are reached after three to four hours. The following metabolic pathway mainly results in two inactive conjugated and hydroxylated metabolites (called metabolites 5 and 6). Metabolites 5 and 6 are mainly excreted in the urine.

Pharmacodynamics

Sibutramine is a neurotransmitter reuptake inhibitor that reduces the reuptake of serotonin (by 53%), norepinephrine (by 54%), and dopamine (by 16%), thereby increasing the levels of these substances in synaptic clefts and helping enhance satiety; the serotonergic action, in particular, is thought to influence appetite. Older anorectic agents such as amphetamine and fenfluramine force the release of these neurotransmitters rather than affecting their reuptake.

Despite having a mechanism of action similar to tricyclic antidepressants, sibutramine has failed to demonstrate antidepressant properties in animal studies.

Contraindications

Sibutramine is contraindicated in:

- ✓ Psychiatric conditions as bulimia nervosa, anorexia nervosa, serious depression or preexisting mania
- ✓ Patients with a history of or a predisposition to drug or alcohol abuse
- ✓ Hypersensitivity to the drug
- ✓ Patients below 18 years of age
- ✓ Concomitant treatment with a monoamine oxidase (MAO) inhibitor, antidepressant or other centrally active drugs, particularly other anoretics
- ✓ Hypertension that is not sufficiently controlled (caution in controlled hypertension)
- ✓ Existing pulmonary hypertension
- ✓ Existing damage on heart valves, coronary heart disease, congestive heart failure, serious arrhythmias, previous myocardial infarction
- ✓ Stroke or transient ischemic attack (TIA)
- ✓ Hyperthyroidism (overactive thyroid gland)
- ✓ Closed angle glaucoma
- ✓ Seizure disorders
- ✓ Enlargement of the prostate gland with urinary retention (relative C.I.)
- ✓ Pheochromocytoma
- ✓ Pregnant and lactating women (relative C.I.)

Side effects

Frequently encountered side effects are: dry mouth, paradoxically increased appetite, nausea, strange taste in the mouth, upset stomach, constipation, trouble sleeping, dizziness, drowsiness, menstrual cramps/pain, headache, flushing, or joint/muscle pain.

Sibutramine can substantially increase blood pressure and pulse in some patients. Therefore all patients treated with sibutramine should have regular monitoring of blood pressure and pulse.

The following side effects are infrequent but serious and require immediate medical attention: cardiac arrhythmias, paresthesia, mental/mood changes (e.g., excitement, restlessness, confusion, depression, rare thoughts of suicide).

Symptoms that require urgent medical attention are seizures, problems urinating, abnormal bruising or bleeding, melena, hematemesis, jaundice, fever and rigors, chest pain, hemiplegia, abnormal vision, dyspnea and edema.

Currently, no case of pulmonary hypertension has been noted, although related compounds (such as Fen-Phen) have shown this rare but clinically significant problem.

The main side effects are noted in 5% of patients; they appear as the arterial hypertension and tachycardia.

Dosage

10 mg once daily (usually in the morning), if this proves insufficient the dose may be increased to 15 mg daily after 4 weeks.

Multiple clinical investigation (STORM, SB1048, BPY 852) has shown that weight loss for >5-10% during a year may be achieved on the basis of 10-15 mg of the preparation per day.

The weigh loss is depend on the dosage of preparation.

Orlistat (marketed under the trade name Xenical by Roche; or over-the-counter as alli by GlaxoSmithKline , like the English word "ally")—also known as tetrahydrolipstatin—is a drug designed to treat obesity. Its primary function is preventing the absorption of fats from the human diet, thereby reducing caloric intake. It is intended for use in conjunction with a physician-supervised reduced-calorie diet.

Orlistat is the saturated derivative of lipstatin—a potent natural inhibitor of pancreatic lipases isolated from the bacterium Streptomyces toxytricini. However, due to simplicity and stability, orlistat rather than lipstatin was developed into an anti-obesity drug.

Pharmacology

Orlistat works by inhibiting gastrointestinal lipase, an enzyme that breaks down triglycerides in the intestine. Without this enzyme, triglycerides from the diet are prevented from being hydrolyzed into absorbable free fatty acids and are excreted undigested. Only trace amounts of orlistat are absorbed systemically; the primary effect is local lipase inhibition within the GI tract after an oral dose. The primary route of elimination is through the feces.

At the standard prescription dose of 120 mg three times daily before meals, orlistat prevents approximately 30% of dietary fat from being absorbed, and about 25% at the standard over-the-counter dose of 60 mg. Higher doses do not produce more potent effects.

It is recommended to take Orlistat during a year - 9 kg of body mass may be reduced during a year and then after the restoration of body weight is not evident.

Efficacy

The amount of weight loss achieved with orlistat varies. In one-year clinical trials, between 35.5% and 54.8% of subjects achieved a 5% or greater decrease in body mass, although not all of this mass was necessarily fat. Between 16.4% and 24.8% achieved at least a 10% decrease in body mass. After orlistat was stopped, a significant number of subjects regained weight—up to 35% of the weight they had lost. Despite this relatively small body mass effect, the XENDOS study found a 37% reduction in the incidence of type 2 diabetes, a significant difference.

Side effects

The primary side effects of the drug are gastrointestinal-related, and include steatorrhea—that is, oily, loose stools; because orlistat blocks some of the dietary fat from being absorbed, the fat is excreted unchanged in the feces, fecal incontinence, frequent or urgent bowel movements, and flatulence. To minimize these effects, foods with high fat

content should be avoided; it is advises to follow a low-fat, reduced-calorie diet. Oily stools and flatulence can be controlled by reducing the dietary fat content to somewhere in the region of 15 grams per meal.

According to investigation, side effects are most severe when beginning therapy and may decrease in frequency with time; this is supported by the results of the XENDOS study, which found that only 36% of people had gastrointestinal adverse effects during their fourth year of taking Orlistat, whereas 91% of study subjects had experienced at least one GI-related side effect during the first year of treatment. It has also been suggested that the decrease in side effects over time may be associated to long-term compliance with a low-fat diet.

Precautions

Absorption of fat-soluble vitamins and other fat-soluble nutrients is inhibited by the use of orlistat. A multivitamin tablet containing vitamins A, D, E, K, and beta-carotene should be taken once a day, at bedtime, when using orlistat.

Contraindications

Orlistat is contraindicated in:

- ✓ Malabsorption
- ✓ Hypersensitivity to Orlistat
- ✓ Reduced gallbladder function (e.g. after cholecystectomy)
- ✓ Pregnancy and breastfeeding

Orlistat should be used caution with: obstructed bile duct, impaired liver function, and pancreatic disease.

THE SURGICAL METHODS

The surgical methods for the treatment of obesity are also learnt. The resection of part of small intestine is performed with the purpose of the nutrient absorption decrease in the intestines and the passage acceleration. The method of vertical banded gastroplasty with “small stomach” formation is also used. As a result of these operations the patients usually lose 20-30 kg of weight, but the further consequences of such operations are not investigated yet. It is known, that in results of such kind of operations the secretion of GI hormones is appreciably changed, that in turn may be attended with the development of the undernourishment syndrome and quite often –results in invalidism.

In the industrialized world, obesity has reached epidemic proportions. Recently it has been declared a major health problem. Keeping a normal weight is a constant battle and to start the fight against obesity is necessary from the childhood. It is possible to single out the patients’ group of risk on the basis of family anamnesis learning, where is necessary to take into consideration not only the evident overweight, but the metabolic common disorder as well: IIT insular diabetes, podagra, arterial hypertension (AH), early cardiovascular complications. The rational diet and physical activity regime should be chosen properly – all of this may help to withstand the risk of obesity formation.

The antagonists of several hormones, produced by the adipose tissue, are currently in the stage of investigation.

By this time there are the possibility to improve the patients’ prognosis by the way of the arterial hypertension compensation, insular diabetes and dislipoproteinemia correction.

In the process of the arterial hypertension treatment the special attention is given to the angiotensinolytic ferment inhibitors.

Obesity stipulates to prescribe the high doses of these preparations, due to their efficiency are connected with penetration into the adipose tissue, which deposits about 40% of renin-angiotensin-aldosteron system activators. Therefore the hydrophilic angiotensin transforming factor’s inhibitors have the great advantage.

The patients with metabolic syndrome, who have apparent neuropathy, the inhibitors of an angiotensin transforming ferment have no alternative, as they impede the undesirable work on the renal tissue by the way of angiotensin II blocking.

Angiotensin II has negative effect on the intrarenal hemodynamics (increasing of the glomerular hypertension), it is the active modulator of inflammation and nephritic fibrosis. The angiotensin transforming ferment inhibitor has neuroprotective effect due to angiotensin II inhibition.

Thereby, treatment of an obesity and metabolic syndrom accordingly, is multicomponent and complicated, as the attending medical has to practice individual and purposeful approach, which claim every doctor and patient efforts and take over a long period of time.

LITERATURE

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Докладът е рецензиран.