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# APPLICATION OF ORLISTAT AND A COMPLEX OF REHABILITATION MEASURES ON VISCERAL OBESITY INDICATORS

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**SUMMARY: The purpose of the study is** to evaluate the effectiveness of the use of orlistat and a complex of rehabilitation measures on indicators of visceral obesity depending on the level of cardiovascular risk (CVR).

**The results of the study** showed dysfunction of adipose tissue and excessive accumulation of visceral fat tissue in high and very high risk patients with both obesity and overweight, and with normal body weight. The established correlations make it possible to predict the intensification of visceral obesity using additional markers of visceral obesity; being simple, easily reproducible and inexpensive, they can be widely used in everyday clinical practice. Assessment of a marker such as apelin 12 can be used to assess and predict the progression of fat metabolism disorders, visceral tissue dysfunction, and can be included together with the assessment of calculated indicators of VAT (IVO, % adipose tissue, visceral fat level according to bioimpedance analysis, HSI and ISP) into the algorithm for examining patients to assess VAT dysfunction and prevent cardiovascular risks. The developed complex of non-drug rehabilitation (diet, physical activity) with patient education at the School of Obesity Prevention in a combination of drugs - orlistat showed a significant more pronounced improvement in indicators of fat metabolism disorders: % adipose tissue, % visceral fat, lipid metabolism indicators: LDL, non-HDL-C, VO indices (IVO, ISP), as well as GC, Apelin-12, and this combination can be recommended for widespread use in practical healthcare.

**Key words:** Visceral obesity, cardiovascular risk. Orlistat.

Obesity is becoming one of the main risk factors for the development and progression of cardiovascular diseases (CVD). The association of high body mass index (BMI) with overall and cardiovascular mortality is confirmed by the results of meta-analyses of numerous prospective studies [1,3]. According to many studies, a connection has been established between the abdominal (android) type of obesity (AbO) and the development of diseases such as type 2 diabetes mellitus (T2DM), arterial hypertension (AH), myocardial infarction and ischemic stroke. Studying the problem of visceral obesity and its impact on cardiovascular risk (CVR) requires the development of diagnostic methods for assessing visceral adipose tissue (3). For a long time, adipose tissue (AT) was considered only as a passive energy depot. It has now been established that adipose tissue is an important endocrine organ and produces a number of biologically active substances (hormones, paracrine factors and cytokines), which are called adipokines. Adipokines are cytokines that are produced by AT and have pleiotropic metabolic effects that play an important pathogenetic role in the development of complications of obesity.

The main tasks in the treatment of obesity are a gradual change in the patient's unhealthy lifestyle, correction of disrupted eating patterns, reducing the dominant role of food

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motivation, and eliminating incorrect connections between emotional discomfort and food intake.

The primary goal is to reduce body weight (BW) by 10% (5–10 kg) within 6 months, which already leads to a reduction in all-cause mortality by 20%, cardiovascular mortality by 9%, cancer mortality by 37% and diabetes-related deaths by 44% [4].

Patients with a BMI over 30 kg/m2 or with a BMI in the range of 27.0–29.9 kg/m2 with cardiovascular or metabolic complications (DM, HTN, DLP) should be prescribed pharmacological therapy. This allows you to maintain the patient's optimal BW value for a long time. Medicines used to reduce BW achieve this effect and act on different mechanisms and pathways. The use of many drugs that effectively reduce body weight has been unsuccessful in clinical practice due to a pronounced negative effect on the cardiovascular system. Currently, the only available and safe drug for the treatment of a wide range of patients with obesity, especially those associated with additional risk factors, or cardiovascular pathology, or metabolic disorders, is the drug orlistat. Orlistat is a drug that acts within the gastrointestinal tract without a negative effect on the central nervous system, which avoids the development of psychological disorders and adverse hemodynamic changes in the heart in the patient [8]. It suppresses the activity of gastric and pancreatic lipases, which inhibits the hydrolysis and absorption of about 30% of dietary fat when taking the drug 120 mg 3 times a day. Because under the influence of food, the secretion of lipases increases; orlistat is recommended to be taken with meals to maximize the suppression of fat absorption. After discontinuation of the drug, its pharmacological effect quickly ceases, and lipase activity is restored. Even in high doses, orlistat does not have a negative effect on other gastrointestinal enzymes (including amylase, trypsin, chymotrypsin and phospholipids). It is very important that orlistat inhibits the absorption of dietary cholesterol in the intestine, regardless of the decrease in BW [8,9,10].

The advantages of the drug include the absence of systemic effects, since it is not absorbed into the blood (acts locally), does not accumulate in the body with long-term use, and has minimal, clinically insignificant interactions with other drugs. Side effects from the gastrointestinal tract while taking orlistat are associated with an error in the diet - eating fatty foods, and not with the drug itself. Discomfort with orlistat is usually transient and usually resolves within the first weeks of therapy when fat intake is limited to 30% of daily calories. On the contrary, the use of orlistat allows the patient to develop new skills in proper eating behavior and aims him at changing his lifestyle and proper nutrition [10,11].

The problem of effectively reducing body weight, adequate blood pressure control, correcting lipid and blood glucose levels, and protecting target organs in order to achieve the lowest possible cardiometabolic risk in an obese patient can be successfully solved with the correct choice of preventive strategy. This strategy should be based on a combination of non-pharmacological methods (diet, physical activity) and drugs - orlistat, which has proven its good clinical efficacy and high level of safety with long-term use. [10,11].

**Objective:** to evaluate the effectiveness of the use of orlistat and a complex of rehabilitation measures on indicators of visceral obesity depending on the level of CVR.

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**Material and methods. Material and methods. A** total of 179 individuals aged 40-70 years without diagnosed CVD (coronary heart disease, chronic heart failure, clinically pronounced atherosclerosis with hemodynamically significant stenosis of the great arteries, etc.) were examined. All patients were distributed depending on the degree of obesity: group 1 with overweight consisted of 27 individuals with BMI = 29.3 ± 1.4 kg/m2, group 2 with 1 degree of obesity consisted of 108 individuals with BMI = 33.9 ± 1 ,3, Group 3 with 2nd degree obesity consisted of 32 individuals with BMI=37.2±2.4 and group 4 with normal body weight and moderate and high CVR according to SCORE-2 consisted of 12 individuals. The control group consisted of 25 healthy individuals with low CVR according to SCORE2 and normal body weight. Cardiovascular risk (CVR) was assessed according to SCORE-2: with low and moderate CVR - 94, with high CVR - 49 individuals, with very high CVR without coronary CVD - 36 individuals. The examination included assessment of anthropometric indicators: body weight BW, height, waist (W) and hip (H) circumference, BMI (BMI=kg/height, m2), W/H ratio; clinical and laboratory parameters: blood pressure, determination of serum total cholesterol, low-density lipoprotein cholesterol-LDL, triglycerides TG, high-density lipoprotein cholesterol-HDL, non-HDL cholesterol = total HDL cholesterol, serum glucose, apelin 12 in blood serum [ 5,6]. The content of apelin-12 in blood plasma was determined by the enzyme immunoassay method using the "Apelin-12 (Human, Rat, Mouse, Bovine) EIA Kit" reagent kit produced by Phoenix Pharmaceuticals (USA) [4,5]. The body composition was assessed using bioimpedance analysis: determination of the percentage of visceral and total fatty tissue. To assess the state of fat metabolism, the following indicators were also used [5,6]:

• visceral obesity index (VII) was calculated according to Amato:

in men - BIR = (waist circumference/39.68 + 1.88×BMI) × (TG/1.03) × (1.31/HDL-C); in women - IVR = (waist circumference/36.58 + 1.89×BMI) × (TG/0.81) × (1.52/HDL cholesterol). (IVO -1.93 normal, 1.94–2.32 slight dysfunction of adipose tissue, 2.32–3.25 moderate dysfunction of adipose tissue, VAI >3.25 high dysfunction of adipose tissue).

• hepatic steatosis index ISP = -3.5856+(0.0141*age) + (0.4711*DM) + (4.4373*OT/Height*100), where DM is present - 1, if DM is not present - 0.

• hepatic steatosis index HSI= 8* ALT/AST+BMI (+2 if T2DM is present, +2 if female). HSI values >36.0 indicate the presence of hepatic steatosis in the patient with a sensitivity of 93.1%, specificity of 92.4% with an accuracy of AUROC of 0.812.

All patients were examined initially and after 3 months of rehabilitation, and were divided into 2 groups: the main group - 72 patients, against the background of a developed complex of rehabilitation program with nutritional correction, physical and psychological rehabilitation within the framework of the School of Obesity Prevention, took orlistat 120 mg (Xenical, pharmaceutical company "F. Hoffmann - La Roche Ltd.", Switzerland) 3 times a day; comparison group - 107 patients who underwent a complex rehabilitation program with nutritional correction, physical and psychological rehabilitation within the framework of the School of Obesity Prevention.

Statistical processing of the research results was carried out using the generally accepted method using a personal computer (Excel 2010 program). The arithmetic mean (M) and the

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error of the arithmetic mean (m) were determined. To determine the statistical significance of differences between the compared indicators, Student's t-test was used.

**Research results and discussion.** When assessing anthropometric parameters, the following were assessed: body weight, height, waist (W) and hip (H) with an assessment of the W/H ratio), BMI. As well as additional data from bioimpedance analysis of body composition: determination of the percentage of visceral and total adipose tissue, biochemical indicators of lipid metabolism disorders, glucose, apelin 12, calculated indicators of visceral obesity. These indicators are presented in Table 1.

**Table 1. Indices of BAT dysfunction, indicators of fat and lipid metabolism in groups depending on the degree of obesity**

| № i/o | Indicators | Control (n=12) | Excess body weight (n=27) | Obesity 1st degree (n=108) | Obesity 2st degree (n=32) | Normal BW (n=12) |
|---|---|---|---|---|---|---|
| 1 | Age, years | 28,5±8,0 | 54±9,8 | 59,3±6,8 | 45,5±4,3 | 38,6±5,2 |
| 2 | CVR by SCORE-2 | 1,25±1,1 | 5,5±7,1 | 10,5±8,7 | 11,5±7,8 | 2,0±1,28 |
| 3 | Body weight (BW) kg | 55,5±8,2 | 88,7±9,0*<br>29,5% | 103,2±13,8<br>39,4% | 119,1±15,2<br>47,5% | 71,08±5,15<br>28,7% |
| 4 | Waist circumference FROM, cm | 78,5±3,0 | 99,6±9,2* | 109,9±10,5* | 118±12,2* | 97,5±6,24 |
| 5 | Hip circumference OB, cm | 99,6±6,3 | 111,8±7,2* | 120,9±7,5* | 127,4±9,1* | 109,9±7,62 |
| 6 | OT/RP ratio | 0,79±0,07 | 0,90±0,07* | 0,91±0,08* | 0,93±0,1* | 0,89±0,07 |
| 7 | BMI | 22,2±2,50 | 29,3±1,4* | 32,6±1,7* | 37,3±1,3* | 24,5±0,86 |
| 8 | % fat tissue | 27,3±7,01 | 40,16±8,01* | 43,4±8,1** | 45,8±5,6** | 39,4±3,28* |
| 9 | Visceral fat (abdominal) | 5,17±1,54 | 11,7±3,1** | 14,5±4,2** | 17,3±4,1** | 11,02±3,11** |
| 10 | THC, mmol/l | 4,8±0,8 | 5,2±0,8 | 5,32±0,8* | 5,75±0,8* | 4,98±0,88 |

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|---|---|---|---|---|---|---|
| 11 | TG, mmol/l | 1,4±0,9 | 1,69±1,01 | 1,81±1,0* | 2,1±1,2* | 1,58±0,71 |
| 12 | LDL, mmol/l | 2,9±0,8 | 3,26±0,9 | 3,41±0,9* | 3,6±0,9* | 2, 8±0,86 |
| 13 | HDL, mmol/l | 1,2±0,2 | 0,9±0,3 | 1,0±0,3 | 1,01±0,3* | 0,97±0,21 |
| 14 | Non-HDL cholesterol, mmol/l | 2,6±0,8 | 2,8±0,8 | 3,52±0,8* | 4,51±0,82* | 4,0±0,9* |
| 15 | IVO | 2,6±0,32 | 3,5±0,3 * | 4,5±0,4** | 5,3±0,5** | 3,15±0,83* |
| 16 | COI | -0,572±0,1 | -0,497±0,15* | -0,395±0,09* | -0,387±0,09* | -0,5±0,18 |
| 17 | HSI | 32,5±4,5 | 36,8±5,3 | 47,3±4,3* | 50,3±6,0* | 35,6±2,36 |
| 18 | Apelin-12, pg/ml | 0,79±0,4 | 3,18±0,55* | 7,09±2,9* | 19,49±8,1* | 5,62±0,8* |

**Note:** * – significant differences, p<0.05, *** p<0.001

An association of BMI indicators in groups 1, 2, 3 with the CVR indicator according to SCORE2 was revealed; a direct correlation (r = 0.68, 0.65 and r = 0.76, respectively). Obesity and overweight are one of the leading causes of CVD and significantly enhance the pathophysiological effect of CVR factors [7].

To assess the state of fat metabolism, special highly specific indicators with regard to cardiovascular risks and mortality were also used, such as: visceral obesity index (VII) calculated according to Amato, liver steatosis indices [1,2].

According to the results of our study, a correlation was identified between the WC/TB ratio and the visceral fat indicator according to bioimpedance analysis of body composition with a correlation coefficient of r = 0.74. According to the literature, there is a strong correlation between BMI and waist circumference values (above 0.80), especially in heterogeneous groups, including both thin individuals and obese patients [7].

Analysis of indicators of VAT dysfunction showed an increase in indicators of visceral adipose tissue, such as IVO, the level of visceral fat according to bioimpedance analysis, HSI and IPI with an increase in the degree of obesity. When comparing functional indicators of obesity, significant differences were established: the indicator of IVO in groups with overweight, 1st degree of obesity, 2nd degree of obesity and normal body weight, but the presence of signs of IVO by 34.6% (p<0.05), 73% (p<0.001), 103.8% (p<0.001) and 21.1% (p<0.05) were higher, respectively, compared to control values. The observed results with an increase in BVR indicate dysfunction of visceral adipose tissue and excessive accumulation of visceral fat. There was a significant increase in body fat % in all groups; even in the group with excess and normal body weight by 47.1% (p<0.05) and 44.3% (p<0.05), respectively, and the level of visceral fat in all groups; even in the group with overweight and normal body weight, it was 126% (p<0.001) and 113% (p<0.001), respectively, higher than in the control, which may be an indicator of visceral obesity in groups even with

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normal body weight. A more significant and reliable increase in % adipose tissue and visceral fat according to bioimpedance analysis of body composition in obese groups: with class 1 obesity by 58.9% ($p<0.001$) and 170.2% ($p<0.001$) and class 2 obesity by 67.7% ($p<0.001$) and 235% ($p<0.001$), respectively, from the control group.

When comparing functional indicators of VAT, significant differences were established: an increase in the HSI indicator in the study groups compared with control indicators, and in groups 1, 2 and 3 amounted to 11.7%, 31% ($p<0.05$) and 35% ($p <0.05$), respectively, compared to the control group. HSI values>36.0 indicate the presence of hepatic steatosis in a patient with a sensitivity of 93.1% and specificity of 92.4% [8]. There was a significant increase in ISP in groups with overweight, grade 1 obesity, grade 2 obesity by 13.1% ($p<0.05$), 30.9% ($p<0.05$), and 32.3% ($p< 0.05$), hepatic steatosis index HSI - in groups with class 1 and class 2 obesity by 45.5% ($p<0.05$) and 54.8% ($p<0.05$), respectively, compared with control indicators.

| | | | | | | |
|---|---|---|---|---|---|---|
| 16 | COI | -0,572±0,1 | -0,497±0,15* | -0,395±0,09* | -0,387±0,09* | -0,5±0,18 |
| 17 | HSI | 32,5±4,5 | 36,8±5,3 | 47,3±4,3* | 50,3±6,0* | 35,6±2,36 |
| 18 | Apelin-12, pg/ml | 0,79±0,4 | 3,18±0,55** | 7,09±2,9** | 19,49±8,1** | 5,62±0,8** |

AO was identified by the WC/TB ratio in 69% of subjects, by BMI, % of adipose tissue and visceral fat in 96% of subjects, which are reliable indicators of lipid metabolism disorders and an independent risk factor for CVD.

According to the results of our study, there was a significant increase in the level of total cholesterol, LDL, non-HDL cholesterol, TG, a decrease in HDL in the group with obesity of 1 and 2 degrees. There was a direct correlation between BMI and non-HDL cholesterol and LDL ($r = 0.86$ and $r = 0.76$, $p<0.05$). Thus, it is possible to judge the disturbance of lipid metabolism in all groups: both overweight, obese, and normal body weight.

One of the new methods for assessing the condition of abdominal adipose tissue is IVO, a marker of BAT dysfunction. In many studies, an increase in indices of BAT dysfunction, such as IVO, the level of visceral fat according to bioimpedance analysis, and the hepatic steatosis index HSI, was associated with a high cardiometabolic risk, both in the general population and in patients without any obvious metabolic disorders [2] .

In obesity, the production of adipokines and the activity of their signaling pathways are altered, which plays an important role in the relationship between obesity, insulin resistance and increased CVR. We studied the role of apelin 12 as a biomarker of BAT dysfunction and increased CVR. Which is consistent with the results of previous studies, apelin is currently being actively studied as a predictor of complications of obesity in various age and gender groups [5,6].

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Analysis of the Apelin 12 index as an early predictor of adipose tissue dysfunction in groups with overweight, grade 1 obesity, grade 2 obesity and normal body weight, but with signs of VO, revealed a significant increase of 306% ($p<0.001$), 797% ($p< 0.001$), 2358% ($p<0.001$) and 611.4% ($p<0.001$), respectively, compared to control values. A high correlation between the apelin 12 indicator and BMI, visceral fat level, CVR according to SCORE-2 according to impedance analysis was revealed with a correlation coefficient $r=0.80$, $r=0.86$, $r=0.70$ ($p<0.05$ ) respectively.

The identified results showed that the assessment of such a marker as apelin 12 can be used to assess and predict the progression of fat metabolism disorders, dysfunction of visceral adipose tissue and can be included together with the assessment of calculated indicators of VAT (IVO, % of adipose tissue, the level of visceral fat according to bioimpedance analysis, HSI and ISP) [5,6,7]. Apelin is an adipokine that is relatively little studied. It is noted that its level increases with obesity and is directly related to the visceral type of distribution of adipose tissue. It was found that plasma apelin concentration significantly increases with increasing degree of abdominal obesity and directly correlates with WC and the ratio of WC to hip circumference (WC/HC) [3].

Evidence of the effectiveness and safety of Xenical (orlistat 120 mg) was obtained in numerous randomized placebo-controlled studies (more than 100 studies in 30 thousand patients) of varying duration (from 7 months to 4 years) [3,7,8].

The problem of effectively reducing body weight, adequate blood pressure control, correcting lipid and blood glucose levels, and protecting target organs in order to achieve the lowest possible cardiometabolic risk in an obese patient can be successfully solved with the correct choice of preventive strategy. This strategy should be based on a combination of non-drug methods (diet, physical activity) with patient education in the School of Obesity Prevention and drugs - orlistat, which has proven its good clinical efficacy and high level of safety with long-term use. The dynamics of indicators during treatment in the main group of patients (rehabilitation program complex + orlistat) are presented in Table 2.

**Table 2. Dynamics of indicators against the background of treatment in the main group (complex rehabilitation program + orlistat)**

| Index | Before treatment | After treatment | % | Reliability, p |
|---|---|---|---|---|
| BMI | 34,35±2,88 | 30,0±2,85 | 12,7 | p<0,05 |
| FROM | 106,0±8,85 | 95,5±6,45 | 9,9 | p<0,05 |
| ABOUT | 115,2±7,6 | 111,7±5,7 | 3 | p>0,05 |
| OT/OB | 0,92±0,07 | 0,88±0,06 | 5,4 | p>0,05 |
| Blood glucose, mmol/l | 6,62±2,25 | 5,86±0,89 | 11,5 | p<0,05 |
| Total cholesterol, cholesterol mmol/l | 5,42±1,14 | 5,08±0,07 | 6,3 | p>0,05 |
| Triglycerides, mmol/l | 1,94±0,99 | 1,76±0,72 | 9,05 | p>0,05 |
| LDL, mmol/l | 3,35±1,1 | 3,0±0,68 | 10,4 | p<0,05 |
| HDL, mmol/l | 1,17±0,22 | 1,04±0,2 | 11,1 | p>0,05 |
| Non-HDL cholesterol | 4,51±1,01 | 3,9±0,84 | 13,5 | p<0,05 |
| Apelin-12 | 26,5±8,31 | 18,5±6,3 | 31,3 | p<0,001 |

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| Homocysteine | 9,61±3,1 | 8,2±2,1 | 14,7 | p<0,05 |
| % fat tissue | 41,58±8,66 | 36,5±4,8 | 14 | p<0,05 |
| % visceral fat | 13,95±4,59 | 12,0±2,9 | 9,5 | p<0,05 |
| IVO | 2,46±0,36 | 2,02±0,17 | 17,8 | p<0,001 |
| COI | 0,04±0,35 | 0,02±0,34 | 50 | p<0,001 |

There was a significant decrease in anthropometric indicators and indicators of body composition in individuals of the 1st group in relation to the comparison group: with a decrease in the ratio of WC, BMI, % of adipose tissue, internal fat by 9.9% (p <0.05), 12. 7% (p<0.05), 14% (p<0.05) and 9.5% (p<0.05), respectively, compared with the indicators of the comparison group (2 groups) - by 4.5% ( p<0.05), 6.0% (p<0.05), 4.5% (p>0.05) and 5.3% (p>0.05), respectively. At the second stage of our study, biochemical parameters of lipid metabolism were assessed.

There was a significant decrease in the biochemical parameters of carbohydrate and lipid metabolism in people of the 1st group in relation to the comparison group: with a decrease in the ratio of blood sugar, LDL, cholesterol-non-HDL, Apelin-12, HC – by 12.7% (p<0. 05), 10.4% (p<0.05), 13.5% (p<0.05), 31.3% (p<0.001) and 14.7% (p<0.05) (Table .2), respectively, compared with the initial indicators; in the comparison group (group 2) – by 6.0% (p<0.05), 4.5% (p>0.05), 7.2% (p>0.05), 4.3% ( p>0.05), 23% (p<0.05) and 12.6 (p<0.05) (Table 3).

**Table 3. Comparison group (rehabilitation program complex)**

| Index | Before treatment | After treatment | % | Reliability, p |
|---|---|---|---|---|
| BMI | 32,7±1,6 | 30,7±1,79 | 6 | p<0,05 |
| FROM | 99,9±8,29 | 95,4±6,7 | 4,5 | p>0,05 |
| ABOUT | 112,7±7,8 | 107±6,2 | 5 | p>0,05 |
| OT/OB | 0,91±0,07 | 0,88±0,07 | 3,3 | p>0,05 |
| Blood glucose, mmol/l | 5,63±0,75 | 5,11±0,95 | 9,2 | p>0,05 |
| Total cholesterol, cholesterol mmol/l | 5,28±1,2 | 5,09±1,14 | 3,6 | p>0,05 |
| Triglycerides, mmol/l | 1,72±0,76 | 1,65±0,89 | 4,1 | p>0,05 |
| LDL, mmol/l | 3,32±1,1 | 3,08±1,14 | 7,2 | p>0,05 |
| HDL, mmol/l | 1,12±0,28 | 1,0±0,31 | 10,7 | p>0,05 |
| Non-HDL cholesterol | 4,16±1,12 | 3,98±1,18 | 4,3 | p>0,05 |
| Apelin-12 | 8,41±4,12 | 6,48±2,62 | 23 | p<0,05 |
| Homocysteine | 6,32±1,1 | 5,52±1,1 | 12,6 | p<0,05 |
| % fat tissue | 40,54±9,46 | 38,7±6,94 | 4,5 | p>0,05 |
| % visceral fat | 11,54±4,51 | 10,92±2,18 | 5,3 | p>0,05 |
| IVO | 1,97±1,33 | 1,65±1,01 | 16,2 | p<0,5 |
| COI | -0,23±0,24 | -0,3±0,24 | 30,4 | p<0,05 |

At the next stage of the study, an analysis of indicators of visceral adipose tissue dysfunction was carried out. An increase in indicators of visceral adipose tissue (VAT) dysfunction, such as VAT, the level of visceral fat according to bioimpedance analysis, liver steatosis index ISP and hepatic steatosis index (HSI). Analysis of indicators of VAT dysfunction showed a decrease in predictors of VO in individuals Group 1 in relation to the comparison group:

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with a decrease in the ratio of IVO and ISP by 17.8% ($p<0.001$) and 50% ($p<0.001$), respectively, compared to the initial indicators in the comparison group (group 2) -. by 16.2% ($p<0.001$) and 30.4% ($p<0.001$) Thus, a complex of non-drug rehabilitation with developed programs of physical rehabilitation and nutrition optimization with patient education at the School of Obesity Prevention in combination with orlistat showed a more pronounced improvement. fat metabolism indicators: BMI, WC, % adipose tissue, % visceral fat, lipid metabolism indicators: LDL, non-HDL cholesterol Apelin-12, HC, VO indices (IVO, ISP).

The findings of our study are confirmed by the results of previous studies. When treating with orlistat, effective reduction of body weight does not require sharp restrictions on the daily calorie intake, since the loss of body weight is almost the same despite varying degrees of calorie restriction. The most intense decrease in body weight with orlistat is observed in the first 3 months. treatment. It was found that weight loss was 5% or more from the initial value over 3 months. – a predictor of long-term and effective results of obesity treatment. Orlistat treatment in obese patients also significantly reduced waist circumference, a criterion for visceral obesity, by more than 8 cm after 1 year [64, 69].

**Conclusion.** The established correlations make it possible to predict the intensification of visceral obesity using additional markers of visceral obesity; being simple, easily reproducible and inexpensive, they can be widely used in everyday clinical practice. Assessment of a marker such as apelin 12 can be used to assess and predict the progression of fat metabolism disorders, visceral tissue dysfunction, and can be included together with the assessment of calculated indicators of VAT (IVO, % adipose tissue, visceral fat level according to bioimpedance analysis, HSI and ISP) into the algorithm for examining patients to assess VAT dysfunction and prevent cardiovascular risks. The developed complex of non-drug rehabilitation (diet, physical activity) with patient education at the School of Obesity Prevention in a combination of drugs - orlistat showed a significant more pronounced improvement in indicators of fat metabolism disorders: % adipose tissue, % visceral fat, lipid metabolism indicators: LDL, non-HDL-C , VO indices (IVO, ISP), as well as GC, Apelin-12, and this combination can be recommended for widespread use in practical healthcare.

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