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Effectiveness of Liraglutide on Metabolic Risk Factors in Obesity Patients

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Yakubov A.V[1]., Saidova Sh.A.[2], Pulatova N.I.[3], Pulatova D.B.[4] , Musayeva L.J[5].

[1]Yakubov Abdujalol Vaxabovich - MD,professor, head of the Department of Clinical Pharmacology, Tashkent Medical Academy;

[2]Saidova Shakhnoza Aripovna - Candidate of Medical Sciences, Senior Teacher Department of Clinical Pharmacology, Tashkent Medical Academy;

[3]Pulatova Nargiza Ikhsanovna - MD, Senior Teacher Department of Clinical Pharmacology, Tashkent Medical Academy;

[4]Pulatova Durdona Bahadirovna - Candidate of Medical Sciences, Senior Teacher Department of Clinical Pharmacology, Tashkent Medical Academy;

[5]Musaeva Lola Jurayevna - Candidate of Medical Sciences, Senior Teacher Department of Clinical Pharmacology, Tashkent Medical Academy;

[6]Abdusamatova Diloram Ziyavutdinovna candidate of medical science, senior teacher of the department of clinical pharmakology of Tashkent Medical Academy

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Abstract

This article analyzes the effectiveness of Liraglutide and its impact on cardiometabolic risk factors in patients with obesity. The effectiveness of Victoza (liraglutide 3.0 mg) was studied in relation to changes in the mass index, body mass, body mass (BM), waist circumference (WC), blood pressure parameters and its effect on cardiometabolic factors. Complex therapy with the use of Liraglutide per day for 3 months is effective for the therapy of obesity and correction of obesity-associated cardiometabolic disturbances.

Being overweight is defined as an abnormal or excessive accumulation of fat that poses a health risk associated with cardiometabolic risk factors for cardiovascular disease and type 2 diabetes mellitus. The catastrophic increase in the prevalence of obesity and its associated diseases, such as type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), etc., is a global medical problem associated with a significantly increased risk of morbidity and mortality.

In addition to adverse health effects, the economic costs associated with obesity are important, ranging from 2 to 7% of total healthcare costs [1, p. 56, 6].

It is known that the risk of obesity-related diseases increases with body mass index (BMI) and is associated mainly with an abdominal and visceral type of obesity, which is a risk factor for T2DM and CVD independent of the degree of obesity [1, p. 57]. The frequency and severity of insulin resistance, which is a key link in the pathogenesis of metabolic syndrome, increase with increasing total body fat mass, especially in the visceral area. Therefore, in the first place, the complex treatment of obesity should take measures aimed at reducing the abdominal and visceral fat mass and related risk factors [1, p. 56, 4, p. 6]

Considering the above, it is extremely important to effectively treat obesity and, undoubtedly, to reduce morbidity and mortality from CVD, DM2 and their complications. Interventions aimed at reducing body weight, and especially visceral fat mass, have a beneficial effect on most of the metabolic disorders associated with obesity. Even a moderate decrease in body weight by 5-10% of the initial weight is already accompanied by a pronounced decrease in the incidence of comorbidities [3, p. 348, 4, p. 6]

As the main causes of obesity are excessive caloric intake combined with a sedentary lifestyle, lifestyle modification based on dietary adjustments and

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increased aerobic physical activity is the basis of treatment. Pharmacotherapy is used to increase the effectiveness of obesity therapy, which allows for more effective weight loss, facilitates the implementation of dietary recommendations, helps to develop new eating habits, and promotes the long-term retention of reduced body weight.

The main objectives of pharmacotherapy are: achievement of clinically significant weight loss (more than 10% of baseline body weight); compensation of existing metabolic disorders; improvement of treatment tolerance; increasing patients' adherence to treatment; prevention of disease recurrence.

Currently, a new drug for the treatment of patients with obesity - Liraglutide 3.0 mg, which is an analogue of human glucagon-like peptide-1 (GLP-1) is registered in Uzbekistan.

Liraglutide (Liraglutide) has 97% homology to the amino acid sequence of endogenous human GLP-1. GLP-1 is a physiological regulator of appetite and food intake. In animal studies, administration of liraglutide resulted in its uptake in specific brain regions, including the hypothalamus, where liraglutide, through specific activation of GLP-1 receptors, increased satiety signals and attenuated hunger signals, thereby promoting weight loss. The pharmacokinetic properties of the drug allow it to be used once a day.

Liraglutide affects a human body weight predominantly by reducing adipose tissue mass by restricting food intake and by regulating appetite by increasing the feeling of a full stomach and satiety while weakening the feeling of hunger and reducing the perceived food intake.

In addition, in individuals with carbohydrate metabolism disorders, liraglutide stimulates insulin secretion and reduces unnecessarily high glucagon secretion in a glucose-dependent manner and improves pancreatic beta cell function, resulting in lower fasting and post-meal glucose concentrations. The mechanism of glucose reduction with GLP-1 agonists also includes a slight delay in gastric emptying, which is more pronounced with short-acting members of this class of incretin drugs.

The results of worldwide long-term clinical trials confirm not only the effectiveness of liraglutide 3.0 mg/day in reducing body weight, but also its positive effect on metabolic parameters [2, p. 322, 5, 1514].

Liraglutide 3.0 mg is indicated as an adjunct to a low-calorie diet and increased physical activity for long-term use to correct body weight in adult patients with BMI:

≥30 kg/m2 (obesity) or ≥27 kg/m2 to <30 kg/m2 (overweight) with at least one associated overweight comorbidity, such as glucose tolerance disorder, type 2 diabetes, arterial hypertension, dyslipidemia or obstructive sleep apnea syndrome.

Contraindications to the use of liraglutide are: hypersensitivity to liraglutide or any of the excipients of the drug; severe renal dysfunction; severe hepatic dysfunction.

Liraglutide is also contraindicated in the following groups of patients and with the following conditions or diseases due to lack of efficacy and safety data: children under 18 years of age; pregnancy and lactation; heart failure III-IV functional class (according to NYHA classification); concomitant use of other weight-loss drugs; concomitant use with insulin; secondary obesity in endocrine diseases or eating disorders, or while taking medications that can cause weight gain.

PURPOSE OF THE INVESTIGATION: to study the efficacy of Victoza (liraglutide 3.0 mg) with respect to changes in body mass index, body weight (BMI), waist circumference (WC), blood pressure parameters and its effect on cardiometabolic risk factors in obese patients.

1. Materials and Methods:

The study was conducted on the basis of 1-clinic of Tashkent Medical Academy. The study included 30 patients (men and women) aged 25 to 59 years with obesity (BMI>30 kg/m2) who signed informed consent to participate in the study.

Exclusion criteria: DM1 and DM2; mental illness, including severe depression, suicidal thoughts or behavior, including a history; taking at the time of inclusion in the investigation any drugs affecting eating behavior; history of cancer; family history of

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medullary thyroid cancer; multiple endocrine neoplasia type 2; pregnancy; drug therapy for obesity (sibutramine and orlistat) at the time of study inclusion and 3 months before inclusion.

During the study, we collected complaints, medical history, and determined anthropometric parameters (height, body weight, waist circumference, BMI).

All patients were treated with Liraglutide 3.0 mg/day (subcutaneous solution 6 mg/ml; cartridge, in a 3 ml syringe pen) after the initial investigations. The initial dose was 0.6 mg/day, followed by standard dose titration according to instructions: the dose was increased by 0.6 mg at intervals of at least one week to improve gastrointestinal tolerance until a therapeutic dose of 3 mg/day was achieved.

All patients were given individual recommendations for a rational diet and physical activity regimen.

The duration of observation and treatment was 3 months, after which a repeat clinical and laboratory examination was performed, as well as an analysis of the efficacy and safety of the therapy.

The following parameters were determined: glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), triglycerides (TG), and liver transaminases (ALT, ACT). Standard oral glucose tolerance test (OGTT) was performed to assess the state of carbohydrate metabolism. At the fasting plasma glycemia level of 6.1 to 6.9 mmol/l we diagnosed increased fasting glycemia, at the plasma glucose level of 7.8 to 11.0 mmol/l at the 120-minute OSGT we had impaired glucose tolerance. All biochemical and hormonal tests were performed in the laboratory of the 1st clinic of the Tashkent Medical Academy.

2. Results and Discussion

The body weight of patients included in the study was 90.0 [82, 100] kg, BMI 36.1 [31.4, 39.3] kg/m2, OT 102 [95.5; 110] cm.

In 46.4% of the patients of the study group, there was a history of diseases, presented mainly by arterial hypertension, controlled against a background of taking various antihypertensive drugs, and dyslipidemia. None of the patients had received medication therapy for obesity at the time of inclusion in the study.

All patients during therapy with Liraglutide 3.0 mg/day noted a significant decrease in appetite, increased feeling of satiety and reduction of food intake. Liraglutide therapy was well tolerated by the patients, the most frequent adverse event was nausea at the beginning of therapy in 10 patients, which was mild and transient. Blood pressure and pulse values in patients during 3 months of Liraglutide therapy at 3.0 mg/day were within the target values.

Dynamics of anthropometric parameters

After 3 months of treatment with Liraglutide 3.0 mg/day, there was a significant decrease in body weight, BMI and OT. The median decrease in MT was 8.3 kg ($p = 0.0016$), BMI was 4.3 kg/m2 ($p = 0.0015$), and OT was 9.0 cm ($p = 0.003$), respectively. All patients achieved clinically significant (≥5%) MT reduction, and 86% of patients reduced MT by more than 10% of baseline. Our results suggest significant efficacy of Liraglutide 3.0 mg/day therapy for 3 months to reduce MT in general and visceral fat mass (indirectly indicated by a significant reduction in OT).

Dynamics of biochemical parameters

The vast majority of the obese patients examined had various metabolic disorders at baseline. At baseline various metabolic disorders were revealed in the vast majority of obese patients: 97.6% of them had dyslipidemia, 46.3% - impaired glucose or impaired glucose tolerance, 97.9% - hyperinsulinemia, 96.8% - insulin resistance, which were usually co-occurring. No DM2 was detected in the examined subjects, according to the data of the OGTT.

After 3 months of therapy with Liraglutide 3.0 mg/day a significant improvement in lipid and carbohydrate metabolism parameters, as well as liver condition was observed.

The most significant positive changes against the background of the complex therapy were revealed in the parameters of carbohydrate metabolism: there was a significant decrease in fasting glycemia by

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9,7% and by 16,296 at the 120th minute of OHCT, serum insulin concentration by 2,0,8% and HOMA-IR index by 32,1% ($p < 0,0001$). These changes are quite natural since they directly reflect the main pharmacological effects of liraglutide: improvement of insulin sensitivity, reduction of hyperinsulinemia and decrease of blood glucose concentration.

Improvement of carbohydrate metabolism in obese patients is an extremely important effect of complex treatment of this category of patients, as it has a preventive value in relation to the development of DM2 and its complications.

According to the literature data, liraglutide 3.0 mg/day has a favorable effect on a number of cardiovascular risk factors, including contributing to positive changes in the blood lipid spectrum. In our study, we obtained results consistent with the literature data: therapy with Liraglutide 3.0 mg/day for 3 months was accompanied by significant favorable changes in the blood lipid spectrum. As a result of treatment, the median level of TC significantly decreased by 0.6 mmol/l (9.7%), LDL cholesterol - by 0.5 mmol/l (13.2%), and TG - by 0.6 mmol/l (25%), ($p < 0.0001$). In addition, there was a trend toward a significant increase in the concentration of HDL (by 18.2%; $p < 0.0001$).

Our results indicate the efficacy of the complex therapy including Liraglutide 3.0mg/day to improve lipid metabolism and, thus, to reduce cardiovascular risk in obese patients. It is important to note that the correlation analysis revealed no significant associations between the improvement of lipid profile and reduction of body weight, BMI and WC, as well as improvement of carbohydrate metabolism parameters, i.e. the positive effect of Liraglutide 3.0 mg on blood lipid spectrum did not depend on the reduction of BMI and glycemic indexes dynamics.

The investigation of liver transaminase levels in our study showed an increase in the activity of enzyme markers of cytolysis initially in 43.6% of examined patients, which is probably due to the presence of nonalcoholic fatty liver disease in obesity. After 3 months of therapy with Victoroza 3,0 mg/day in patients with obesity, a significant decrease in serum activity of hepatic transaminases was observed: median ALT concentration decreased by 16.6 units/l (31.9%; $p < 0.0001$), and ACT - by 8.2 units/l (21.9%; $p < 0.0001$). In general, after 3 months of therapy, ALT and ACT levels normalized in all patients.

Based on the analysis of the parameters of carbohydrate and lipid metabolism, as well as the activity of liver transaminases, we can conclude that therapy with Victorza 3.0 mg/day in combination with lifestyle modification is effective for the prevention and correction of existing disorders of lipid and carbohydrate metabolism associated with visceral obesity.

3. Conclusion

Thus, the complex therapy with Liraglutide 3.0 mg/day for 3 months is effective for the treatment of obesity and correction of obesity-associated cardiometabolic disorders, since it promotes the clinically significant reduction of body weight and body fat and, moreover, leads to improvement of carbohydrate and lipid metabolism parameters.

Treatment including Liraglutide is well tolerated, safe, and effective in terms of influencing the key pathophysiological basis of obesity - abdominal obesity and insulin resistance, which together contribute to the reduction of overall cardiometabolic risk and improve prognosis in this category of patients.

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