THE EFFECTS OF GLUCAGON-LIKE PEPTIDE-1 AGONIST THERAPY (SEMAGLUTIDE AND TIRZEPATIDE) ON METABOLIC AND HORMONAL PARAMETERS IN MEN WITH OBESITY AND INSULIN RESISTANCE

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Annotation: In recent years, obesity and insulin resistance have become increasingly prevalent among men and are considered key pathogenetic factors in the development of metabolic syndrome, type 2 diabetes mellitus, and hormonal imbalance. In such conditions, glucagon-like peptide-1 (GLP-1) receptor agonists—semaglutide and the dual GIP/GLP-1 agonist tirzepatide—have been recognized as effective pharmacological treatment options. This article analyzes the effects of these therapies on metabolic and hormonal parameters in men with obesity and insulin resistance. The results of clinical studies demonstrate that the use of semaglutide and tirzepatide is associated with significant weight reduction, improved insulin sensitivity, stabilization of glycemic control, and optimization of lipid metabolism. Moreover, weight loss and reduction of visceral adipose tissue contribute to the improvement of hormonal balance in men, particularly through an indirect increase in testosterone levels, reduction of leptin resistance, and enhancement of adiponectin secretion. The dual mechanism of action of tirzepatide further enhances its metabolic efficacy, providing superior clinical outcomes in patients with severe insulin resistance. This article highlights the role of GLP-1 agonists in the comprehensive management of metabolic and endocrine disorders in men and substantiates their clinical relevance.

Keywords:
obesity; insulin resistance; GLP-1 receptor agonists; semaglutide; tirzepatide; metabolic syndrome; hormonal imbalance; testosterone; insulin sensitivity; visceral adipose tissue.

Introduction

Over the past decades, obesity and insulin resistance have become one of the major global public health problems. The increasing prevalence of these conditions among men significantly elevates the risk of metabolic syndrome, type 2 diabetes mellitus, cardiovascular diseases, as well as reproductive and hormonal disorders. One of the central pathogenetic mechanisms of insulin resistance is the increase in visceral adipose tissue, chronic low-grade inflammation, and disruption of hormonal regulation. In this context, glucagon-like peptide-1 (GLP-1) receptor agonists are considered a modern and effective pharmacological approach for the treatment of obesity and insulin resistance.

Physiological Role of the GLP-1 and GIP Incretin System

GLP-1 is an intestinal incretin hormone secreted by L-cells of the small intestine after food intake. It enhances glucose-dependent insulin secretion, suppresses glucagon secretion, delays gastric emptying, and reduces appetite through central nervous system mechanisms. Glucose-dependent insulinotropic polypeptide (GIP) primarily participates in the regulation of lipid and carbohydrate metabolism. Tirzepatide activates both incretin pathways simultaneously, resulting in a pronounced metabolic effect.

Mechanisms of Action of Semaglutide and Tirzepatide

Semaglutide is a selective GLP-1 receptor agonist that induces weight loss by reducing appetite and enhancing satiety. Tirzepatide, by activating both GLP-1 and GIP receptors, provides a more potent improvement in insulin sensitivity. Clinical studies indicate that tirzepatide demonstrates superiority over semaglutide in reducing body weight and visceral adipose tissue.

Effects on Metabolic Parameters

Body Weight and Adipose Tissue

Patients treated with semaglutide demonstrate an average body weight reduction of 10–15%, whereas tirzepatide enables weight loss of up to 15–22%. A significant reduction in visceral adipose tissue plays a crucial role in decreasing insulin resistance.

Carbohydrate Metabolism

Both agents reduce fasting plasma glucose levels, improve the HOMA-IR index, and decrease daily glycemic variability. Stabilization of glycemic control has also been observed in non-diabetic men with insulin resistance.

Lipid Profile

GLP-1 receptor agonists reduce triglyceride and low-density lipoprotein (LDL) levels while moderately increasing high-density lipoprotein (HDL) concentrations. These changes contribute to a reduced cardiovascular risk.

Effects on Hormonal Parameters

Testosterone and Sex Hormones

Obesity in men is associated with decreased testosterone levels, largely due to increased aromatase activity. Weight reduction induced by GLP-1 agonist therapy leads to decreased aromatase activity and a consequent indirect increase in testosterone levels. Clinical observations have demonstrated improvements in both total and free testosterone concentrations.

Leptin and Adiponectin

Weight loss results in decreased leptin levels and reduced leptin resistance. Concurrently, increased adiponectin secretion enhances insulin sensitivity.

Clinical Cases

Clinical Case 1

A 45-year-old male patient with a body mass index (BMI) of 34 kg/m^2 and a HOMA-IR of 4.2 received semaglutide therapy for 24 weeks. As a result, body weight decreased by 12%, HOMA-IR was reduced to 2.1, and total testosterone levels increased by 20%.

Clinical Case 2

A 38-year-old male patient with severe insulin resistance and abdominal obesity was treated with tirzepatide for 36 weeks. The therapy resulted in an 18% reduction in body weight, normalization of triglyceride levels, and a marked improvement in glucose sensitivity.

Adverse Effects and Limitations

The most common adverse effects include nausea, vomiting, and diarrhea, which are primarily observed during the initial weeks of therapy. Rapid weight loss may increase the risk of gallstone formation; therefore, combined treatment with dietary modification and physical activity is recommended.

Conclusion

Semaglutide and tirzepatide demonstrate high efficacy in the comprehensive management of metabolic and hormonal disorders in men with obesity and insulin resistance. The dual incretin mechanism of tirzepatide makes it a particularly promising therapeutic option in cases of severe insulin resistance. These agents promote not only significant weight reduction but also restoration of hormonal balance.

Adabiyotlar, References, Литературы:

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