WEB OF SCIENTIST: INTERNATIONAL SCIENTIFIC RESEARCH JOURNAL
ISSN: 2776-0979, Volume 6, Issue 2, February- 2025

ASSESSMENT OF THE CARDIOPROTECTIVE EFFICACY OF DULAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Sadikova Nigora Gayratovna
Candidate of Medical Sciences

Ashurova Nazifa Gayratovna
Postgraduate Specialist in Endocrinology
Tashkent Medical Academy

Abstract

According to the latest data from the FDA (Food and Drug Administration), approximately 537 million people worldwide are affected by diabetes (98% of them with type 2 diabetes). By the year 2045, this number is expected to reach 783 million. A new promising class of drugs, known as Glucagon-like peptide-1 receptor agonists (GLP-1 RA), has entered modern medicine. These drugs, when used as monotherapy or in combination with other hypoglycemic agents (such as metformin or basal insulin), have demonstrated high efficacy in treating type 2 diabetes. One representative of the GLP-1 RA class is dulaglutide (Trulicity), which is administered once weekly as a subcutaneous injection at a dose of 1.5mg/0.5ml. This innovative drug helps control postprandial glycemia, reduces the risk of cardiovascular diseases (CVD), and does not cause hypoglycemic episodes.According to the clinical study results during a three-month, dulaglutide treatment (1.5mg), the fasting blood glucose level in the observation group decreased to 7.5±1.04mmol/l, while postprandial glucose dropped to 10.3±1.05mmol/l.Glycated hemoglobin (HbA1c) was reduced to 7.8 ± 0.5% after three months.Triglyceride (TG) levels decreased by 21.4%, from 4.2±0.5mmol/l.Low-density lipoprotein (LDL) levels were reduced by 27%, from 4.8 ± 0.75mmol/l, resulting in a positive change in lipid profile.Systolic blood pressure (SBP) reached the target level of 125.0±5.0mmHg, while diastolic blood pressure (DBP) decreased to 90±5mmHg.Body mass index (BMI) was reduced from 27.3±2.1 kg/m² to 25.4±1.5kg/m² after treatment, indicating weight loss in patients.

Keywords: Dulaglutide, GLP-1 RA, cardiovascular system, type 2 diabetes mellitus, glycated hemoglobin (HbA1C)

Introduction

Diabetes mellitus (DM) is a noninfectious epidemic that concerns the global medical community. It is particularly dangerous due to its ability to cause irreversible

pathological changes in vital organs, including the cardiovascular system, kidneys and nerve cells, as a result of chronic hyperglycemia. According to the World Health Organization (WHO), diabetes mellitus leads to approximately 6.7 million deaths worldwide each year, with at least 50% of these deaths attributed to cardiovascular complications [12].Diabetes itself increases the risk of cardiovascular diseases by 2 to 4 times. Moreover, a body mass index (BMI) exceeding 25 kg/m² further worsens disease prognosis [3].

Currently, type 2 diabetes mellitus (T2DM) cannot be adequately managed solely with glucose-lowering drug therapies. Given the dysfunction of pancreatic beta cells and the persistent hyperglycemia involved in diabetes pathogenesis, a multifactorial approach incorporating cardiometabolic and nephroprotective therapies is increasingly necessary in clinical practice to mitigate the damage to target organs.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) have demonstrated significant clinical benefits in multiple studies, including AWARD, REWIND, SUSTAIN, and LEADER trials. These studies confirm that GLP-1 RA exhibit superior efficacy compared to other hypoglycemic drugs, with minimal side effects, high safety profiles, low risk of hypoglycemia and few contraindications.

Since 2020, leading medical associations such as the American Diabetes Association (ADA), the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD) have recommended GLP-1 RA as first-line treatment options for patients with type 2 diabetes mellitus. This recommendation is independent of glycemic control levels and aims to reduce cardiovascular risk factors in diabetic patients [1,4,15].

In 2020, dulaglutide, a GLP-1 receptor agonist (GLP-1 RA), was approved by the U.S. Food and Drug Administration (FDA) for the treatment of type 2 diabetes mellitus (T2DM). In the same year, due to its cardioprotective effects, dulaglutide was also officially recognized as a drug that reduces cardiovascular risk factors, regardless of the presence or absence of preexisting cardiovascular diseases in patients with T2DM [13].Dulaglutide exerts its effects through multiple mechanisms:postprandial glucose control in a glucose-dependent manner,reduction of glycated hemoglobin (HbA1c),proliferation of pancreatic beta cells,suppression of hepatic gluconeogenesis, leading to improved glycemic control and furthemore,appetite suppression via hypothalamic satiety center activation, delaying gastric emptying and contributing to weight loss.Anti-inflammatory effects on vascular endothelium, reducing low-density lipoprotein (LDL) cholesterol and inhibiting atherosclerotic progression, thereby supporting cardioprotective outcomes [5].

The REWIND trial included 9,901 patients with type 2 diabetes mellitus (mean age: 66.2 years). Patients were divided into two groups:dulaglutide group (N = 4,949): received 1.5 mg of dulaglutide and placebo group (N = 4,952).Patients were monitored for an average of 5.4 years. Among them, 1257 patients already had cardiovascular disease, while the rest had varying degrees of cardiovascular risk factors.The study results demonstrated that dulaglutide reduced major cardiovascular complications by 12% compared to placebo [6,7,8].

Objective

To evaluate the efficacy of dulaglutide in reducing cardiovascular disease (CVD) risk in patients with type 2 diabetes mellitus (T2DM).

Materials and Methods

A total of 20 patients (mean age: 56.7±2.2 years) with T2DM and either preexisting cardiovascular diseases (CVD) or a high risk of cardiometabolic complications were selected for the study.

Patients received weekly subcutaneous injections of dulaglutide (1.5mg) for three months, in combination with other hypoglycemic agents, including metformin or sodium-glucose co-transporter-2 (SGLT-2) inhibitors.At baseline, the following clinical parameters were assessed:fasting plasma glucose (FPG),postprandial plasma glucose (PPG),glycated hemoglobin (HbA1c),body mass index (BMI),lipid profile (triglycerides and low-density lipoproteins [LDL]) and systolic and diastolic blood pressure (SBP and DBP)

At the end of the study, the same parameters were reassessed to evaluate the impact of dulaglutide therapy on metabolic and cardiovascular risk factors.

Results

The study included 20 patients (mean age: 56.7±2.2 years) diagnosed with type 2 diabetes mellitus (T2DM) and either preexisting cardiovascular disease (CVD) or a high risk of cardiometabolic complications. Among them, 12 were female and 8 were male.

At baseline, carbohydrate metabolism parameters were assessed in all 20 patients, revealing the following values:fasting plasma glucose (FPG): 9.0±1.04 mmol/l,postprandial plasma glucose (PPG): 12±2.05mmol/l,glycated hemoglobin (HbA1c): 9.05±0.5%.To evaluate the weight-reducing effects of dulaglutide, the baseline body mass index (BMI) was recorded, showing an average of 27.3 ± 2.1kg/m².Lipid metabolism parameters were also assessed at the beginning of the

study: triglycerides (TG): 4.2±0.5mmol/l; low-density lipoproteins (LDL-C): 4.8± 0.75mmol/l.

To investigate the effects of dulaglutide on hemodynamic parameters, the following baseline blood pressure values were recorded: systolic arterial blood pressure (SBP): 145.6 ±5.3mmHg and diastolic arterial blood pressure (DBP): 100.4 ±9.8mmHg.

For three months, patients received weekly subcutaneous injections of dulaglutide (1.5mg) either as monotherapy or in combination with oral hypoglycemic agents such as metformin or sodium-glucose co-transporter-2 (SGLT-2) inhibitors.

Table 1. Carbohydrate metabolism changes in patients with Type 2 Diabetes on dulaglutide therapy

Parameters	Before treatment n=20 n=20	After treatment n=20n=20
Fasting blood glucose mmol/l	9,0 ±1,04	7,5±1.04
HbA1C,%	9,05±0,5	7,8±0,5
Glucose(postprandial)mmol/l	12±2,05	10,3±1,05*

A significance level of *p ≤ 0.05 indicates that the observed differences in clinical parameters after treatment, compared to baseline values, are statistically significant and not due to random variation.

In 20 patients with type 2 diabetes mellitus (T2DM), the following glycemic improvements were observed after 3 months of dulaglutide therapy: fasting blood glucose decreased by 16.7% , postprandial blood glucose reduced by 14.17%, glycated hemoglobin (HbA1C) decreased by 13.81%, reaching the target level.

Table 2. Changes in lipid metabolism in Patients with Type 2 Diabetes on dulaglutide therapy

Parameters	Before treatment n=20n=20	After treatment, n=20
BMI, kg/m²	27,3±2,1	25,4±1,5
TG,mmol/l	4,2±0,5	3,3±0,5*
LDL,mmol/l	4,8±0,75	3,5±0,4*

A significance level of *p ≤ 0.05 indicates that the observed differences in clinical parameters after treatment, compared to baseline values, are statistically significant and not due to random variation.

As seen in Table 2, patients experienced a reduction in appetite while on dulaglutide therapy, leading to a significant 7% decrease in body weight. The average BMI decreased from 27.3±2.1 kg/m² to 25.4±1.5 kg/m² after treatment.Compared to baseline measurements:Triglyceride (TG) levels decreased by 21.4% ,Low-density lipoprotein (LDL) levels reduced by 27% .These improvements contributed to a more favorable lipid profile, reducing the risk of atherosclerosis.

Hemodynamic parameters also showed positive changes: Systolic arterial blood pressure (SBP) decreased from 125.0±5.0 mmHg by 14.2% . Diastolic arterial blood pressure (DBP) decreased from 90.0±5.0 mmHg by 10.36% .These reductions indicate an improvement in cardiovascular health, achieving target blood pressure levels.

Adverse Effects and Safety Profile: 30% of patients experienced mild gastrointestinal side effects (nausea, diarrhea, bloating) during the first 3 weeks, but these symptoms resolved with continued treatment. No significant changes in liver enzyme levels were observed. Baseline values: Alanine aminotransferase (ALT): 28±5 U/L ,Aspartate aminotransferase (AST): 22±3 U/L .After 3 months of dulaglutide therapy, liver function remained stable. No hypoglycemic episodes were recorded, confirming the safety of the medication.

Conclusions

1. In patients with type 2 diabetes, a 3-month course of dulaglutide (1.5mg) improved the glycemic profile by reducing fasting blood glucose by 16.7%, postprandial glucose by 14.17%, and glycated hemoglobin (HbA1C) by 13.81%.
2. By lowering harmful lipid metabolism markers—low-density lipoproteins (LDL) by 27% and triglycerides by 21.4%, dulaglutide helped prevent atherosclerosis while achieving a 7% reduction in body weight. Additionally, it had a positive impact on hemodynamic parameters, reducing systolic blood pressure (SBP) by 14.2% and diastolic blood pressure (DBP) by 10.36%, thereby demonstrating its efficacy in reducing cardiovascular disease risk.
3. The study results confirm that dulaglutide is an effective and safe medication for use in patients with type 2 diabetes.

References:

1. American Diabetes Association: Clinical practice recommendations.//Diabetes Care.2023
2. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes. Diabetes Care. 2021;44(Suppl. 1):S111–S124.
3. Bhascaran K et al. Lancet Diabetes Endocrinol 2018;6:944-53.
4. И.И. Дедова, М.В. Шестаковой, А.Ю. Майорова. 11-й выпуск.Алгоритмы специализированной медицинской помощи больным сахарным диабетом 2023;26(2S):1-157.
5. Greenspan F.S., Gardner D.G. Greenspan's Basic and Clinical Endocrinology. New York: McGraw-Hill Medical; 2011.
6. Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet. 2019;394:121-130.
7. Gerstein HC, Colhoun HM, Dagenais GR, et al. Design and baseline characteristics of participants in the Researching cardiovascular Events with a Weekly Incretin in Diabetes (REWIND) trial on the cardiovascular effects of dulaglutide. Diabetes Obes Metab. 2018; 20:42-49.
8. Konig M, Riddle MC, Colhoun HM, et al. Exploring potential mediators of the cardiovascular benefit of dulaglutide in type 2 diabetes patients in REWIND. Cardiovasc Diabetol. 2021;20:194.
9. Nevola R, Epifani R, Imbriani S, et al.: GLP-1 receptor agonists in non-alcoholic fatty liver disease: current evidence and future perspectives. Int J Mol Sci. 2023, 24.
10. Nauck MA, Quast DR, Wefers J, Pfeiffer AF: The evolving story of incretins (GIP and GLP-1) in metabolic and cardiovascular disease: a pathophysiological update. Diabetes Obes Metab. 2021, 23:5-29.
11. Pratley RE, Aroda VR, Lingvay I, Lüdemann J, Andreassen C, Navarria A, Viljoen A: Semaglutide versus dulaglutide once weekly in patients with type 2 diabetes (SUSTAIN 7): a randomised, open-label, phase 3b trial. Lancet Diabetes Endocrinol. 2018, 6:275-286.
12. Press release WHO March,1. 2024
13. Trulicity. [Summary of Product Characteristics]. Houten, The Netherlands: Eli Lilly and Company; 2015.
14. Trulicity (dulaglutide) is the first and only type 2 diabetes medicine approved to reduce cardiovascular events in adults with and without established cardiovascular

disease" Eli Lilly and Company (Press release). 21 February 2020. Retrieved 23 February 2020.
15. The European Association for the Study of Diabetes (EASD)

Ashurova Nazifa Gayrat qizi
Tashkent ,Yashnabad ,Izzat street-34
ashurovanazifa2507@gmail.com
+998997032115