Trends in Oncology Vol 6 Issue 1 2024
DOI: 10.37155/2717–5278–0601–1

Original Research Article

Open Access

Omniscient Pte.Ltd.

Observation of the Clinical Efficacy of Metformin and Pioglitazone in the Treatment of Type 2 Diabetes Mellitus Complicated with Coronary Heart Disease

Elias Abula, Shan Gao*

Department of Endocrinology, Shaanxi Provincial People's Hospital, Xi'an 710068, Shaanxi Province, China

***Correspondence to:** Shan Gao. Shaanxi Provincial People's Hospital, No. 256, Youyi West Road, Xi'an City 710068, Shaanxi Province, China; Email: gutongse123@163.com.

How to cite: Elias Abula, Shan Gao. Observation of the Clinical Efficacy of Metformin and Pioglitazone in the Treatment of Type 2 Diabetes Mellitus Complicated with Coronary Heart Disease. *Trends in Oncology*, 2024; 6(1). Doi: 10.37155/2717-5278-0601-1.

Abstract: Objective: To analyze the application effects of metformin and pioglitazone in the treatment of type 2 diabetes mellitus (T2DM) complicated with coronary heart disease (CHD). **Methods:** A total of 82 patients with T2DM and CHD from November 2022 to November 2023 were selected for the study. Using a random number table, they were evenly divided into a control group (41 cases treated with pioglitazone) and an observation group (41 cases treated with a combination of metformin and pioglitazone). The clinical efficacy of the two groups was compared. **Results:** The incidence of adverse reactions in both groups was basically the same ($P > 0.05$); the observation group showed significantly lower rates of complications, fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), glycated hemoglobin (HbA1c), homeostasis model assessment of insulin resistance (HOMA-IR), total cholesterol (TC), triglycerides (TG), and Gensini score than the control group ($P < 0.05$). **Conclusion:** Compared with monotherapy, the combined use of pioglitazone and metformin can enhance the clinical efficacy in treating T2DM complicated with CHD, regulate lipid indicators, and has potential for promotion.

Keywords: Metformin; Pioglitazone; Type 2 diabetes mellitus; Coronary heart disease

Diabetes mellitus (DM) is the third leading cause of death, following cardiovascular diseases as the first and cancer as the second. Type 2 diabetes mellitus (T2DM) is the most common, accounting for over 90% of cases. T2DM is a metabolic disorder characterized by chronic hyperglycemia and impaired insulin function and secretion, affecting multiple organs. In recent years, the incidence of T2DM has increased, often accompanied by macrovascular or microvascular complications, with coronary heart disease (CHD) being one of them[1]. The UK Prospective Diabetes Study (UKPDS) has shown that effective blood glucose control can prevent endpoint events, with a 1% reduction in HbA1c leading to a

21% reduction in the likelihood of complications. For those with concurrent CHD, drug therapy is often employed, and metformin, which enhances tissue glucose utilization and inhibits hepatic glucose output, is commonly used[2]. Pioglitazone, a thiazolidinedione, is also an insulin sensitizer that improves insulin sensitivity, effectively controlling blood glucose. There is limited research on the combined use of these two drugs in treating this complication. This study focuses on patients with T2DM and CHD, analyzing the application effects of combination therapy.

1. Data and Methods

1.1 General Information

Between November 2022 and November 2023, we conducted a study on 82 patients with Type 2 Diabetes Mellitus (T2DM) and Coronary Heart Disease (CHD) at our hospital. Using a random number table, the patients were evenly divided into a control group and an observation group. The control group comprised 41 patients, including 23 males and 18 females, with ages ranging from 32 to 74 years and an average age of (52.28±3.33) years. The observation group also had 41 patients, including 22 males and 19 females, with ages ranging from 33 to 75 years and an average age of (52.34±3.30) years. There were no statistically significant differences in general information between the two groups ($P > 0.05$), ensuring comparability.

Inclusion Criteria: Patients who met the diagnostic criteria for T2DM[3] and CHD[4], were able to communicate effectively, and provided informed consent for participation in the study.

Exclusion Criteria: Patients with a history of mental illness, old or acute myocardial infarction, allergies to the study drugs, or significant organ dysfunction were excluded.

1.2 Methods

Both groups received dietary and exercise control and did not use any other antidiabetic drugs. The control group was treated with pioglitazone (Hangzhou Zhongmei Huadong Pharmaceutical; NMPA approval number H20060664): a dosage of 30mg was administered orally once a day for a duration of 6 months. The observation group was treated with a combination of metformin (Qilu Pharmaceutical; NMPA approval number H37020561): a dosage of 0.5g was administered orally three times a day for a duration of 6 months.

1.3 Observation Items and Indicators

Evaluation of Glycemic Indicators[5]: Venous plasma samples were collected, and FPG and 2hPG were measured using the hexokinase method. HbA1c was examined using the immunoturbidimetric method. Evaluation of Insulin, Lipids, and Coronary Artery Lesions[6]: HOMA-IR, TC, and TG were assessed in both groups. The severity of coronary artery lesions was evaluated using the Gensini score, where a higher score indicates more severe lesions. Safety Evaluation: Complications included renal dysfunction, edema, and anemia. Adverse reactions included diarrhea, abdominal pain, and nausea.

1.4 Statistical Methods

Data were processed using SPSS 27.0. Quantitative data are expressed as ($\bar{x}$±s), and categorical data as (%). The t and x^2 test were conducted, and a significance level of $P < 0.05$ was considered statistically significant.

2. Results

2.1 Comparison of Glycemic Indicators between the Two Groups

After treatment, both groups showed significant reductions in FPG, 2hPG, and HbA1c compared to before treatment, with more pronounced changes observed in the observation group ($P < 0.05$). See details in (**Table 1**).

2.2 Comparison of Insulin, Lipids, and Coronary Artery Lesions between the Two Groups

After treatment, both groups showed significant reductions in HOMA-IR, TC, TG, and Gensini scores compared to before treatment, with more pronounced changes observed in the observation group ($P < 0.05$). See details in (**Table 2**).

2.3 Comparison of Safety between the Two Groups

The incidence of adverse reactions was generally similar between the two groups ($P < 0.05$), while there was a difference in the incidence of complications between the two groups ($P < 0.05$). See details in (**Table 3**).

Table 1: Comparison of Glycemic Indicators between the Two Groups [n($\bar{x}$±s)]

group	instances	FPG (mmol/L)		2hPG (mmol/L)		HbA1c (%)	
		before treatment	after treatment	before treatment	after treatment	before treatment	after treatment
Observation	41	9.91±1.12	6.45±1.11[a]	15.11±1.17	7.71±1.03[a]	9.31±1.11	6.61±0.41[a]
Control	41	9.93±1.08	7.61±1.13[a]	15.26±1.09	8.83±1.05[a]	9.35±1.05	7.21±0.52[a]
t	/	0.082	4.689	0.601	4.876	0.171	5.802
P	/	0.935	0.000	0.550	0.000	0.864	0.000

Note: Compared to before treatment in this group, [a]P < 0.05 (significant).

Table 2: Comparison of Insulin, Lipids, and Coronary Artery Lesions between the Two Groups [n($\bar{x}$±s)]

Indicators	Time	Observation Group (n = 41)	Control Group (n = 41)	t	P
HOMA-IR	before treatment	6.61±1.02	6.63±1.00	0.090	0.929
	after treatment	3.00±0.25[a]	3.31±0.21[a]	6.080	0.000
TC (mmol/L)	before treatment	9.25±1.13	9.29±1.07	0.165	0.870
	after treatment	5.81±1.24[a]	7.51±1.06[a]	6.673	0.000
TG (mmol/L)	before treatment	3.52±0.22	3.56±0.20	0.861	0.392
	after treatment	1.81±0.21[a]	2.91±0.23[a]	22.615	0.000
Gensini (points)	before treatment	37.52±4.16	37.63±4.29	0.118	0.906
	after treatment	14.78±3.25[a]	20.41±4.16[a]	6.829	0.000

Note: Compared to before treatment in this group, [a]P < 0.05 (significant).

Table 3: Comparison of Safety between the Two Groups [n(%)]

group	instances	Adverse Reactions				Complications			
		Diarrhea	Abdominal Pain	Nausea	Incidence Rate	Renal Dysfunction	Edema	Anemia	Incidence Rate
Observation	41	1	1	1	4.88	1	1	0	4.88
Control	41	0	1	1	7.32	4	4	2	24.39
x^2	/	/	/	/	0.213	/	/	/	6.248
P	/	/	/	/	0.644	/	/	/	0.012

3. Discussion

Patients with type 2 diabetes mellitus (T2DM) often experience endocrine disruptions, and poorly controlled blood sugar levels can lead to various complications, including diabetic nephropathy and atherosclerosis. In T2DM, the body produces insulin, but the tissues do not respond adequately, affecting insulin function. Notably, not all insulin is ineffective. Studies have shown that some T2DM patients produce a large amount of insulin that cannot exert its effects, leading to insulin deficiency. Appropriate medications are needed to stimulate insulin production, enhance its effects, or activate its function. The typical pathological features of T2DM include β-cell failure and insulin resistance. Prolonged research has shown that insulin resistance affects oxidative stress, lipid disorders, obesity, and compromises endothelial cell function, leading to hyperhomocysteinemia and promoting a prothrombotic state [7]. Coronary heart disease (CHD) poses a threat to health, and multiple studies indicate a significant impact of diabetes on CHD. The coexistence of these two diseases increases the incidence of abnormalities such as dyslipidemia, heart failure, and hypertension, leading to an elevated mortality rate. Compared to the healthy population, individuals with T2DM have a 2-4 times higher probability of developing CHD. Even with conventional treatment, T2DM patients aged 50-60 are at an increased risk of CHD with higher mortality rates. The occurrence of this complication is influenced by multiple factors, including prolonged high blood sugar levels leading to abnormalities in nitric oxide systems and vasodilators, hypertension, and chronic inflammation affecting vascular smooth muscle cell proliferation. Hypertension, T2DM has a

high probability of complications from hypertension, which is the basis for atherosclerosis; inflammation, the effects of chronic and long-term inflammation, lead to further proliferation of vascular smooth muscle cells, *etc*.[8] For patients with this comorbidity, previous approaches often involved a stepwise treatment, combining dietary control, exercise, and antidiabetic medications.

In the clinical treatment of type 2 diabetes mellitus (T2DM) combined with coronary heart disease (CHD), prevention is crucial. Patients should prioritize smoking cessation, alcohol moderation, weight reduction, and limitation of overall calorie intake, especially avoiding high-fat foods. Effective glycemic control, along with the regulation of dyslipidemia, can effectively prevent macrovascular complications. Since patients often present with abnormal lipid levels, controlling lipid levels during treatment is essential The choice of appropriate medication is a key aspect of clinical treatment for T2DM combined with CHD. Metformin is widely used, and its extensive application in T2DM patients enhances tissue insulin utilization, increases glucose utilization, impedes abnormal hepatic glycogen formation, reduces hepatic glucose output, inhibits glucose uptake in intestinal wall cells, and significantly increases insulin-mediated glucose metabolism. Metformin is involved in the entire glucose metabolism process, promoting anaerobic glycolysis and providing protection to pancreatic islet beta cells, preventing damage and effectively controlling disease progression over the long term. It acts on the intestines, inhibiting glucose absorption, reducing blood glucose levels, lowering HbA1c, preventing microvascular complications, and also preventing myocardial infarction. Additionally, it helps control patient weight and improve lipid levels.[9] Analyzing the hypoglycemic mechanism of metformin, it primarily affects the mitochondria of liver cells, influencing oxidative processes. Liver cells are affected, resulting in decreased lactate intake, reduced glucose content, decreased hepatic glucose neoformation, and increased blood lactate levels. Metformin acts on insulin-sensitive tissues such as adipocytes, skeletal muscles, and the liver, regulating intracellular calcium metabolism and significantly enhancing sensitivity to insulin in peripheral tissues. With an oral administration, metformin has an absorption rate of about 50%, a plasma half-life of approximately 2 hours, and is almost unbound in plasma, with most excreted through urine. Studies suggest that metformin not only regulates lipid profiles but also alleviates vascular inflammation, corrects endothelial cell disorders, and prevents macrovascular diseases. Metformin can protect the cardiovascular system by reducing blood glucose levels, regulating diastolic cardiac function, improving lipid levels, and alleviating oxidative stress. The International Diabetes Federation (IDF) recommends metformin as a first-line drug in the clinical treatment of T2DM.

Pioglitazone, when employed, effectively combats diabetes and enhances insulin sensitivity. It is a *PPARr* agonist that, upon administration, reaches the liver and peripheral tissues, promoting an increase in insulin sensitivity. It activates *PPARr* at various sites, including the liver, skeletal muscles, and adipose tissue, improving the transcription of insulin-responsive genes. This involvement spans glucose physiological activities, encompassing processes such as generation, transport, and utilization. Pioglitazone can reduce blood glucose levels, lower insulin resistance, and concurrently regulate endothelial function, improving glucose and lipid metabolism.[10] With a high absolute bioavailability of 99%, pioglitazone, when administered orally, can be detected in the blood within 0.5 hours on an empty stomach, reaching peak levels at 2 hours. Postprandial administration delays peak levels by 3-4 hours. Pioglitazone's plasma half-life ranges from 3 to 7 hours. It primarily binds to serum proteins and undergoes metabolism through oxidation and hydroxylation. Research confirms that pioglitazone acts on the liver and body tissues, reinforcing insulin resistance, reducing hepatic glucose output, and effectively controlling blood glucose levels. It improves various metabolic processes related to lipids, regulates genes associated with glucose control, and modulates their transcription.

The combination of the two drugs, metformin and pioglitazone, demonstrates enhanced therapeutic efficacy, effectively regulating lipid metabolism, and alleviating the burden of T2DM combined with CHD. The results of this study reveal that, compared to the control group, the observation group exhibited lower levels of FPG, 2hPG, and HbA1c ($P < 0.05$), indicating that the combination therapy can control blood glucose

levels and alleviate the condition. The observation group also showed lower levels of HOMA-IR, TC, TG, and Gensini scores ($P < 0.05$), suggesting that combination therapy can regulate lipid levels, reduce insulin resistance, and improve coronary artery lesions. The lower incidence of complications in the observation group ($P < 0.05$) indicates that combination therapy can prevent complications, reducing the likelihood of kidney damage, anemia, and other complications. The comparable rates of adverse reactions between the two groups ($P > 0.05$) suggest that combined drug therapy does not increase adverse reactions, ensuring its safety. This finding is consistent with the results of Xue Lijun's study, further supporting the safety and efficacy of combined drug therapy. This shows that combined medication can effectively alleviate T2DM combined with CHD, promote disease improvement, improve endocrine function, and promote the improvement of physiological functions.

In summary, compared to monotherapy, the combination of pioglitazone enhances clinical efficacy in T2DM combined with CHD, regulating lipid indicators and holding significant potential for broader application.

References:

[1] Liu Jun, Yang Xinyi, Xu Yixin, Shao Jiaqing, Ye Xiaozhen. Liraglutide combined with metformin in the treatment of a patient with type 2 diabetes complicated with coronary heart disease in 10 years [J]. *Chinese Journal of Diabetes*, 2023, 15(1): 54-58 .

[2] Cai Junling. Application advantages of liraglutide combined with metformin in the clinical treatment of type 2 diabetes complicated with coronary heart disease [J]. *Diabetes New World*, 2023, 26(12):81-84.

[3] Kang Jie, Zhang Jianjian, Zhang Weidong, Zhang Yue, Huang Gaode. Observation on the efficacy and safety of nicorandil combined with metformin in the treatment of patients with type 2 diabetes and coronary heart disease [J]. *International Medical and Health Herald*, 2023, 29(7):936-939.

[4] Li Wenzheng. Evaluation of the clinical effect of liraglutide combined with metformin in the treatment of type 2 diabetes complicated with coronary heart disease [J]. *Diabetes New World*, 2023, 26(7):80-83.

[5] Yu Ruihua. Analysis of the effectiveness of metformin plus insulin glutathione in the treatment of type 2 diabetes complicated with coronary heart disease [J]. *Diabetes New World*, 2023, 26(7):99-102.

[6] Sun Xiaodong, Mo Yuhua, Han Lu. Analysis of the clinical effect of metformin and pioglitazone in the treatment of type 2 diabetes complicated with coronary heart disease [J]. *Diabetes New World*, 2023, 26(6): 65-68.

[7] Chen Yan, Wang Hao, Wei Xueli. Effects of acarbose combined with metformin on glucose metabolism, inflammatory factors and cardiovascular events in patients with type 2 diabetes and coronary heart disease [J]. *Journal of Chronic Diseases*, 2023, 24(2): 315-317.

[8] Wei Dayong. Effect of metformin hydrochloride and dapagliflozin in the treatment of elderly patients with type 2 diabetes and coronary heart disease [J]. *Diabetes New World*, 2022, 25(17):91-93+97.

[9] Guo Jianping, Wei Qin, Peng Danping, Yan Dien, Xiao Liming, Zhou Xiaozhi, Wang Meili, Zheng Huanhuan, Fu Jinxiang, Liu Jinping, Xiao Weiping. Alogliptin combined with metformin and glimepiride on elderly patients with type 2 diabetes and coronary heart disease Comparison of the effects of blood sugar fluctuations[J]. *Journal of Rational Clinical Drug Use*, 2022, 15(24):53-56.

[10] Zhao Xiaotao, Sun Ying. Analysis of the clinical effect of metformin and pioglitazone in the treatment of type 2 diabetes complicated with coronary heart disease [J]. *Practical Clinical Integration of Traditional Chinese and Western Medicine*, 2021, 21(17): 25-26.