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Effects of semaglutide on islet function in patients with type 2 diabetes mellitus

ZHOU Yanling*, JIANG Hui, HONG Xin, TONG Deyin, CAO Shengkun

*Department of Pharmacy, Jiangsu Province (Suqian) Hospital, Suqian, Jiangsu 223800, China

Corresponding author: CAO Shengkun, E-mail: dvuamxa854@163.com

Abstract: **Objective** To investigate the efficacy of semaglutide in treating patients with type 2 diabetes mellitus（T2DM）and its effects on islet function, serum microRNA（miR）- 146a and miR - 351. **Methods** A total of 180 patients with T2DM admitted to Jiangsu Provincial（Suqian）Hospital from February 2023 to January 2024 were selected. They were randomly divided into a control group（n=90）and an observation group（n=90）. The control group received metformin and empagliflozin tablets, while the observation group received the same treatment along with semaglutide for 90 days. Relevant indicators, such as blood glucose, blood lipids, islet function, miR-146a, and miR- 351 levels, as well as therapeutic efficacy and adverse reactions, were measured and recorded before and after treatment. **Results** After treatment, the observation group showed lower levels of blood glucose（fasting blood glucose, 2-hour postprandial blood glucose, and glycosylated hemoglobin）, blood lipids（triglyceride, total cholesterol, low- density lipoprotein cholesterol）, and islet function [fasting insulin, homeostasis model assessment of insulin resistance（HOMA-IR）] compared to the control group（P<0.05）. The homeostasis model assessment of pancreatic β-cell function index, and high-density lipoprotein cholesterol in the observation group were significantly higher those in the control group（P<0.05）. After treatment, the serum level of miR-146a in the control group was significantly lower than that in the observation group（1.80±0.57 *vs* 2.25±0.66, t=4.895, P<0.01）, and miR-351 levels were significantly higher than that in the observation group（4.11±1.47 *vs* 3.50±1.54, t=2.718, P=0.007）. The total effective rate in the observation group was 94.44%, significantly higher than the 82.22% in the control group（$\chi 2$=5.367, P=0.020）. **Conclusion** Semaglutide treatment shows significant efficacy in T2DM patients by regulating the levels of miR-146a and miR-351, restoring islet function, reducing blood glucose and lipids, and ensuring high safety.

Keywords: Semaglutide; Type 2 diabetes mellitus; Metformin; Empagliflozin; microRNA; miR-146a; miR-351; Islet function

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With aging and the decline of metabolic function, the incidence of diabetes has gradually increased, which is particularly prominent in the middle-aged and elderly population. Due to the decline of physical and metabolic functions in this group, the insulin secretion mechanism is disturbed, thereby increasing the risk of developing diabetes, among which type 2 diabetes mellitus (T2DM) occupies a dominant position. According to statistics, T2DM accounts for more than 95% of all diabetes types [1], and it is the main cause of increased complication risks and mortality in diabetic patients [2]. The pathological characteristics of T2DM include decreased levels of glucagon-like peptide-1 (GLP-1), dyslipidemia, and significant insulin resistance [3]. If these pathological conditions are not effectively improved, they will lead to persistent hyperglycemia, which in turn promotes the occurrence of complications such as atherosclerosis, diabetic retinopathy, diabetic foot, and diabetic peripheral neuropathy, seriously affecting the quality of life and prognosis of patients.

As a GLP-1 receptor agonist, semaglutide has shown significant efficacy in lowering blood glucose and controlling body weight in recent years [4]. With the in-depth development of molecular biology research, microRNAs (miRNAs), as a class of gene expression regulators, have attracted increasing attention for their roles in the development of diabetes and its complications. Among them, miR-351 is specifically upregulated in high-fat-induced diabetic mouse models [5], while miR-146a is downregulated in patients with diabetic retinopathy [6]. Based on these findings, it is speculated that the serum levels of miR-351 and miR-146a may reflect the disease state of T2DM and play important roles in disease progression. Therefore, this study aims to investigate the therapeutic effect of semaglutide on T2DM patients by observing its impacts on serum miR-351, miR-146a, and islet function, hoping to provide new scientific evidence for the treatment of T2DM patients.

1 Materials and Methods

1.1 General Information

A total of 180 T2DM patients admitted to Suqian Hospital of Jiangsu Provincial People's Hospital from February 2023 to January 2024 were selected as research subjects and randomly divided into a control group (90 cases) and an observation group (90 cases). Inclusion criteria:Conforming to the diagnostic criteria for T2DM [7]; Aged over 45 years; Body mass index (BMI) ≥ 24 kg/m²; Complete clinical data. Exclusion criteria: Allergy to semaglutide; Existing obvious infections; Being in the acute phase of cardiovascular and cerebrovascular diseases; Complicated with malignant tumors, hematological system diseases, or autoimmune system diseases; Pregnant or

lactating women. This study was approved by the Ethics Committee of Suqian Hospital of Jiangsu Provincial People's Hospital (Ethics Approval No.: 2024-SL-0182), and all research subjects provided informed consent. There were no statistically significant differences in age, gender, BMI, and duration of diabetes between the two groups (P>0.05). See **Table 1.**

Tab.1 Comparison of general data between the two groups (n=90, $\bar{x}\pm s$)

Group	Male/Female (case)	Age (years)	BMI (kg/m²)	Duration of diabetes (years)
Control group	48/42	64.50±6.32	25.72±3.10	8.60±2.90
Observation group	46/44	63.97±6.40	25.61±3.02	8.73±2.54
χ^2/t value	0.089	0.559	0.241	0.320
P value	0.765	0.577	0.810	0.749

1.2 Treatment Methods

Patients in the control group were treated with metformin and empagliflozin tablets (Hangzhou Zhongmei Huadong Pharmaceutical Co., Ltd., National Medicine Approval No. H20213448, specification: each tablet contains 500 mg metformin hydrochloride and 5 mg empagliflozin), administered during or after meals, 1 tablet per time, twice a day. Patients in the observation group received combined treatment with semaglutide (Novo Nordisk, National Medicine Approval No. SJ20210014, specification: 1.5 mg/mL) on the basis of the above treatment. The initial dose of semaglutide was 0.25 mg per time, administered by subcutaneous injection. After 4 weeks of treatment, the dose was adjusted to 0.5 mg per time, once a week. Both groups of patients received continuous treatment for 90 days.

1.3 Observation Indicators

1.3.1 Efficacy Evaluation Criteria [8]

Marked efficacy: Clinical symptoms and vital signs tend to be normal, and blood glucose decreases to the normal level. Effective: Clinical symptoms and vital signs are improved, and blood glucose level is significantly reduced. Invalid: Diabetic symptoms are not improved or even aggravated. Total effective rate = (number of cases with marked efficacy + number of effective cases) / total number of cases × 100%.

1.3.2 Detection of Serum miR-146a and miR-351

Fasting venous blood (5 mL) was collected from patients in both groups before treatment and at the end of treatment, respectively. Serum was obtained by low-temperature centrifugation, aliquoted, and stored for later use. Total serum RNA was extracted using the Trizol method (Thermo Fisher Scientific, USA). Reverse transcription of cDNA was performed using a reverse transcription kit (Thermo Fisher Scientific, USA), and qRT-PCR amplification was carried out using the SYBR®Premix Ex Taq™ kit (Takara, Japan). The relative expression levels of miR-146a and miR-351 in serum were calculated using the $2^{-\Delta\Delta Ct}$ method. Primers for miR-146a, miR-351, and U6 were all synthesized by RiboBio Co., Ltd. (Guangzhou, China).

miR-146a forward sequence: 5′-TGA GAA CTG AAT TCC ATG GGT T-3′; reverse sequence: 5′-GCT GTC AAC GAT ACG CTA CGT AAC G-3′.

miR-351 forward sequence: 5′-ACA CTC CAG CTG GTC CCT GAG GAG CCC GG-3′; reverse sequence: 5′-CTC AAC TGG TGT CGT GGA GTC GGC AAT TCA GTT GAG TCA GGC TC-3′.

U6 forward sequence: 5′-AAG GTG AAG CTG GGA GTC AAC-3′; reverse sequence: 5′-GGG GTC ATT GAT GGC AAC AAT A-3′.

1.3.3 Detection of Blood Glucose, Blood Lipids, and Islet Function

Fasting blood (5 mL) was collected from patients in the control group and the observation group the next day before treatment and after 90 days of treatment, respectively. The blood samples were centrifuged at 3,000 r/min (centrifugal force: 1,000×g). Fasting plasma glucose (FPG), 2-hour postprandial blood glucose (2hPG), glycosylated hemoglobin (HbA1c), triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were detected using an automatic biochemical analyzer (Beckman Coulter Model DX800). Fasting insulin (FINS), homeostasis model assessment of insulin resistance (HOMA-IR), and homeostasis model assessment of pancreatic beta-cell function (HOMA-β) were measured using an automatic biochemical analyzer (Roche Cobas-6000).

1.3.4 Adverse Drug Reactions

During the treatment period of the two groups, adverse reaction events were counted, mainly including nausea, diarrhea, headache, and hypoglycemia.

1.4 Statistical Methods

Statistical analysis was performed using SPSS 24.0 software. Categorical variables were expressed as cases (%), and analyzed using the chi-square test. Continuous variables conforming to the normal distribution were expressed as $\bar{x}\pm s$, and analyzed using the t-test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Evaluation of Clinical Efficacy in the Two Groups

The total effective rate of the observation group was 94.44%, which was significantly higher than 82.22% of the control group, with a statistically significant difference (P<0.05). See **Table 2**.

2.2 Comparison of Blood Glucose Levels Between the

Two Groups

Compared with the control group, FPG, 2hPG, and HbA1c in the observation group were significantly decreased after treatment (P<0.05). See **Table 3**.

Tab.2 Comparison of treatment efficacy between the two groups of patients [n=90, case(%)]

Group	Invalid	Marked Efficacy	Effective	Total Effective Rate (%)
Control group	16(15.56)	45(44.44)	29(27.78)	82.22
Observation group	5(6.67)	55(61.11)	30(32.22)	94.44
χ^2 value				5.367
***P* value**				0.020

2.3 Comparison of Blood Lipid Levels Between the Two Groups

After treatment, TC, TG, and LDL-C in the observation group were significantly lower than those in the control group, while HDL-C was higher than that in the control group (P<0.05). See **Table 4**.

2.4 Comparison of Islet Function Indicators Between the Two Groups

After treatment, HOMA-β in the observation group was significantly higher than that in the control group (P<0.05), while FINS and HOMA-IR were significantly lower than those in the control group (P<0.05). See **Table 5**.

2.5 Comparison of Serum miR-146a and miR-351 Levels Between the Two Groups

After treatment, the level of miR-146a in the observation group was higher than that in the control group (P<0.05), while the level of miR-351 was lower than that in the control group (P<0.05). See **Table 6**.

2.6 Occurrence of Adverse Reactions

In the control group, 2 cases of nausea, 1 case of diarrhea, 2 cases of headache, and 2 cases of hypoglycemia occurred. In the observation group, 2 cases of nausea, 1 case of headache, and 1 case of hypoglycemia occurred. There was no statistically significant difference in the total incidence of adverse reactions between the control group and the observation group (7.78% *vs* 4.44%, χ^2=0.871, P=0.350).

Tab. 3 Comparison of blood glucose indicators between two groups of patients before and after treatment (n=90, $\bar{x}\pm s$)

Group	FPG(mmol/L)		2 h PG(mmol/L)		HbA1c(%)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control group	9.50±1.91	6.64±0.54[a]	13.50±2.65	8.31±0.69[a]	8.72±0.84	6.56±0.73[a]
Observation group	9.42±1.86	6.20±0.70[a]	13.40±2.39	7.30±0.82[a]	8.66±0.93	5.58±0.69[a]
***t* value**	0.285	4.772	0.266	8.941	0.454	9.256
***P* value**	0.776	<0.001	0.791	<0.001	0.650	<0.001

Note: Compared with before treatment in the same group, [a]P<0.05.

Tab. 4 Comparison of blood lipid levels between two groups of patients (n=90, $\bar{x}\pm s$)

Group	TC(mmol/L)		TG(mmol/L)		LDL-C(mmol/L)		HDL-C(mmol/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control group	5.53±1.20	4.35±0.65[a]	3.15±0.90	1.76±0.82[a]	4.32±0.30	2.63±0.42[a]	1.18±0.26	1.50±0.28[a]
Observation group	5.48±1.28	3.89±0.68[a]	3.10±0.94	1.20±0.76[a]	4.40±0.38	2.11±0.30[a]	1.15±0.23	1.31±0.25[a]
***t* value**	0.270	4.639	0.364	4.752	1.568	9.558	0.820	4.044
***P* value**	0.787	<0.001	0.716	<0.001	0.119	<0.001	0.413	<0.001

Note: Compared with before treatment in the same group, [a]P<0.05.

Tab. 5 Comparison of pancreatic islet function indicators between two groups of patients (n=90, $\bar{x}\pm s$)

Group	FINS（μU/mL）		HOMA-IR		HOMA-β（%）	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Control group	16.79±4.70	14.95±3.81	5.20±1.19[a]	4.16±1.01	34.20±10.27[a]	60.26±18.17[a]
Observation group	17.06±4.85	12.89±3.30	5.10±1.16[a]	3.48±0.90	34.50±10.19[a]	73.32±20.15[a]
***t* value**	0.379	3.169	0.571	4.769	0.197	4.566
***P* value**	0.705	0.002	0.569	<0.001	0.844	0.009

Note: Compared with before treatment in the same group, [a]P<0.05.

Tab.6 Comparison of miR-146a and miR-351 between two groups of patients before and after treatment (n=90, $\bar{x}\pm s$)

Group	miR-146a		miR-351	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Control Group	0.80±0.17	1.80±0.57[a]	6.31±2.01	4.11±1.47[a]
Observation Group	0.83±0.19	2.25±0.66[a]	6.35±1.90	3.50±1.54[a]
***t* value**	0.116	4.895	0.137	2.718
***P* value**	0.266	<0.001	0.891	0.007

Note: Compared with before treatment in the same group, [a]P<0.05.

3 Discussion

T2DM is a metabolic disease characterized by long-term hyperglycemia caused by insulin deficiency or impaired insulin biological activity, often accompanied by various metabolic disorders. The early symptoms of T2DM do not show the typical "polyuria, polydipsia, polyphagia, and weight loss", so it is very easy to cause missed diagnosis. Studies have shown that the increase in the number of T2DM patients worldwide is related to factors such as overweight and obesity, and its mechanism may be their own insulin resistance [9]. At present, drugs such as metformin, empagliflozin, and liraglutide are commonly used in clinical treatment [10]. However, long-term use of a single drug will lead to increased drug resistance of the body and decreased therapeutic effect [11]. Therefore, exploring more comprehensive and effective drugs is of great significance for the treatment of T2DM patients and the improvement of their prognosis.

As an enterogenic hormone secreted by the intestine, semaglutide is a new type of long-acting GLP-1 analog. It mainly acts on pancreatic β-cells to promote insulin synthesis and secretion, reduce hepatic glucose release, enhance insulin sensitivity, act on the hypothalamus to inhibit appetite, and achieve the effect of lowering blood glucose through the above-mentioned effects, which has a good therapeutic effect on diabetes [12]. Relevant studies have also confirmed that semaglutide combined with metformin and empagliflozin tablets has a significant therapeutic effect on T2DM patients [13-14]. This study also found that the total effective rate of semaglutide combined with metformin and empagliflozin in the treatment of T2DM patients was significantly higher than that of metformin and empagliflozin alone, and there was no statistically significant difference in the incidence of adverse reactions. The above results indicate that semaglutide has a good therapeutic effect and high safety in the treatment of T2DM patients.

Studies have revealed that GLP-1 receptor agonists can reduce the levels of TG, TC, and LDL-C by regulating lipoprotein release from intestinal epithelial cells and fat decomposition, which shows that semaglutide has the ability to indirectly regulate blood lipid levels [15]. A study by Zhang Fengli et al. [16] also confirmed that semaglutide has the effects of lowering blood glucose and blood lipids. FINS, HOMA-IR, and HOMA-β are important indicators commonly used in medicine to evaluate islet function. HOMA-IR reflects the level of insulin resistance in the body; the higher the index, the lower the sensitivity of the body to insulin and the more severe the degree of insulin resistance. HOMA-β reflects the function of pancreatic β-cells. Pancreatic β-cells are the main cells secreting insulin in the pancreas, responsible for regulating insulin secretion according to the blood glucose level of the body. In addition, studies have revealed that semaglutide combined with metformin and empagliflozin tablets can reduce the levels of FPG, 2hPG, HbA1c, and HOMA-IR in obese T2DM patients, while increasing the level of HOMA-β, suggesting that semaglutide may lower blood glucose by restoring islet function [17]. This study found that the levels of FPG, 2hPG, HbA1c, TC, TG, LDL-C, FINS, and HOMA-IR in the observation group were significantly lower than those in the control group, while the levels of HDL-C and HOMA-β were significantly higher than those in the control group, suggesting that semaglutide may reduce blood glucose and blood lipid levels and improve T2DM by restoring islet function.

miRNAs play important roles in the occurrence and development of T2DM. Studies have found that miR-146a is involved in the development of diabetes, and its dysregulated expression accelerates the progression of diabetes [18]. miR-146a exerts its functions in various physiological processes through negative regulation of signal transduction and immune responses. Chen Lin [19] observed in the serum of patients with gestational diabetes mellitus that compared with the insulin resistance group, the level of miR-146a in the extreme and severe insulin resistance groups was significantly decreased, suggesting that miR-146a may be related to insulin resistance. The reason may be that when the level of miR-146a is too low, islet dysfunction is prone to occur, which in turn aggravates insulin resistance. Studies have also found that low expression of miR-146a can promote the high expression of inflammatory factors, exacerbate the inflammatory response of the body, and cause the occurrence and development of chronic diseases such as hyperglycemia and hyperlipidemia [20]. On the other hand, miR-351 has also been found to be closely related to diabetes and its complications. A study by Badacz et al. [21] revealed that miR-351 can affect the processes of glycolipid synthesis, decomposition, and transport by targeting and regulating genes and signaling pathways related to glycolipid metabolism (such as AMPK, PPARγ, etc.), indicating that miR-351 may be related to lipid synthesis. Studies have pointed out that miR-351 regulates the development of carotid atherosclerosis by negatively regulating glycolipid metabolism, promoting inflammatory responses, and inducing cell apoptosis [22]. In addition, animal experiments have shown that in the transcriptome of diabetic mice, miR-351 is specifically upregulated in diabetic mice induced by high lipids, suggesting that the upregulation of miR-351 may play a promoting role in the progression of diabetes and atherosclerosis [22]. This study found that after treatment, the level of miR-146a in the observation group was significantly higher than that in the control group, while the level of miR-351 was significantly lower than that in the control group, suggesting that semaglutide may promote the recovery of islet function, thereby reducing glycolipid secretion and improving insulin resistance by regulating the levels of miR-146a and miR-351.

In conclusion, semaglutide combined with metformin and empagliflozin tablets has a significant therapeutic effect on T2DM. It may improve islet function, reduce insulin resistance, and then lower blood glucose and blood lipid levels by regulating the abnormal expression of miR-146a and miR-351. However, this study also has some limitations: the sample size is relatively small, and the sample size should be expanded in the follow-up. The specific mechanism of semaglutide in the treatment of

T2DM needs to be further explored. Future research can focus on the regulatory effect of semaglutide on miRNAs and its long-term impact on islet function, hoping to provide a more comprehensive basis for the treatment of T2DM.

Conflict of interest None

Reference

[1] Yoon HS, Cho CH, Yun MS, et al. *Akkermansia muciniphila* secretes a glucagon-like peptide-1-inducing protein that improves glucose homeostasis and ameliorates metabolic disease in mice[J]. Nat Microbiol, 2021, 6(5): 563-573.

[2] Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment[J]. Lancet Diabetes Endocrinol, 2014, 2(8): 634-647.

[3] Nolen-Doerr E, Stockman MC, Rizo I. Mechanism of glucagon-like peptide 1 improvements in type 2 diabetes mellitus and obesity[J]. Curr Obes Rep, 2019, 8(3): 284-291.

[4] Lu WT, He JR, Chen WY. Adverse drug event signal mining of semaglutide based on FDA Adverse Event Reporting System database[J]. China Pharm, 2022, 33(15): 1865-1869, 1875. **[In Chinese]**

[5] Li HP, Fan JH, Zhao YR, et al. Nuclear miR-320 mediates diabetes-induced cardiac dysfunction by activating transcription of fatty acid metabolic genes to cause lipotoxicity in the heart[J]. Circ Res, 2019, 125(12): 1106-1120.

[6] Chen SD, Yuan ME, Liu YM, et al. Landscape of microRNA in the aqueous humour of proliferative diabetic retinopathy as assessed by next-generation sequencing[J]. Clin Exp Ophthalmol, 2019, 47(7): 925-936.

[7] Chinese Diabetes Society. Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020 edition)[J]. Chin J Diabetes Mellit, 2021, 13(4): 315-409. **[In Chinese]**

[8] Guan ZA. Modern diabetes[M]. Tianjin: Tianjin Scientific & Technical Publishers, 2020:461-465.. **[In Chinese]**

[9] Chilunga FP, Henneman P, Meeks KA, et al. Prevalence and determinants of type 2 diabetes among lean African migrants and non-migrants: the RODAM study[J]. J Glob Health, 2019, 9(2): 020426.

[10] Jing Y, Shi J, Lu B, et al. Association of serum lipocalin-2 level with cardiovascular disease in patients with type 2 diabetes[J]. Chin J Endocrinol Metab, 2021, 37(4): 267-273. **[In Chinese]**

[11] Ye J, Chen D, Qiu ZH, et al. Efficacy of smaglutide combined with dapagliflozin and metformin in patients with obese type 2 diabetes mellitus and nonalcoholic fatty liver disease[J]. Diabetes New World, 2024, 27(1): 19-22. **[In Chinese]**

[12] Gan XJ, Zhan LQ. The effect of ultra-early rehabilitation nursing intervention on limb function recovery and quality of life in elderly patients with ischemic stroke [J]. Jilin Med J, 2023, 44(4): 1134-1137. **[In Chinese]**

[13] Xu QC, Qin PR, Xu DM. The impact of the combination of semaglutide and dapagliflozin on type 2 diabetes mellitus patients with poor response to metformin therapy[J]. Med Innov China, 2024, 21(27): 70-75. **[In Chinese]**

[14] Wang Y, Tu ZX, Liao HP, et al. Clinical efficacy of semaglutide combined with empagliflozin and metformin in the treatment of obese patients with newly diagnosed type 2 diabetes mellitus[J]. Chin J Clin Ration Drug Use, 2024, 17(27): 18-21. **[In Chinese]**

[15] Okamoto A, Yokokawa H, Nagamine T, et al. Efficacy and safety of semaglutide in glycemic control, body weight management, lipid profiles and other biomarkers among obese type 2 diabetes patients initiated or switched to semaglutide from other GLP-1 receptor agonists[J]. J Diabetes Metab Disord, 2021, 20(2): 2121-2128.

[16] Zhang FL, Zhang DF, Zhao YN, et al. Effect of semaglutide on cardiovascular risk factors in patients with type 2 diabetes mellitus[J]. China Med, 2022, 17(12): 1800-1803. **[In Chinese]**

[17] Lu HB, Ma YJ, Li LP, et al. Efficacy analysis of semaglutide combined with dapagliflozin and metformin in obese patients with diabetes[J]. Clin Res, 2024, 32(10): 73-76. **[In Chinese]**

[18] Yang KW, Qiang Z, Jin BF, et al. Regulatory effect of miR-146 on diabetic cardiomyopathy[J]. Chin J Pathophysiol, 2018, 34(11): 1947-1952. **[In Chinese]**

[19] Chen L. Relationship between serum miR-146a expression and insulin resistance in patients with gestational diabetes mellitus[J]. J Pract Med Tech, 2022, 29(3): 279-282, 337. **[In Chinese]**

[20] Fumimoto C, Yamauchi N, Minagawa E, et al. miR-146a is mutually regulated by high glucose-induced oxidative stress in human periodontal ligament cells[J]. Int J Mol Sci, 2024, 25(19): 10702.

[21] Badacz R, Przewłocki T, Legutko J, et al. microRNAs associated with carotid plaque development and vulnerability: the clinician's perspective[J]. Int J Mol Sci, 2022, 23(24): 15645.

[22] Han Q, Zhu W, Wang XH, et al. Research progress of miR-638 in diabetic nephropathy[J]. Mil Med J South China, 2020, 34(8): 591-593. **[In Chinese]**

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·论　著·

司美格鲁肽对2型糖尿病患者胰岛功能的影响

周艳玲[1]，　江慧[1]，　洪馨[2]，　童德银[1]，　曹胜焜[1]

1. 江苏省人民医院宿迁医院药学部，江苏 宿迁 223800；2. 江苏省人民医院宿迁医院急诊科，江苏 宿迁 223800

摘要：目的　探讨司美格鲁肽治疗2型糖尿病(T2DM)患者的疗效和对胰岛功能、血清微小RNA(miR)-146a、miR-351的影响。**方法**　选取2023年2月至2024年1月于江苏省人民医院宿迁医院收治的180例T2DM患者，将其随机分为对照组(n=90)和观察组(n=90)。对照组采用二甲双胍恩格列净片治疗，观察组则在对照组的基础上联合司美格鲁肽治疗，连续治疗90 d，检测并记录治疗前后的相关指标(血糖、血脂、胰岛功能、miR-146a、miR-351水平、疗效和不良反应)。**结果**　治疗后，观察组血糖(空腹血糖、餐后2 h血糖、糖化血红蛋白)、血脂(三酰甘油、总胆固醇、低密度脂蛋白胆固醇)水平及胰岛功能[空腹胰岛素、稳态模型评估胰岛素抵抗指数(HOMA-IR)]均低于对照组(P<0.05)。观察组稳态模型评估胰岛β细胞功能指数、高密度脂蛋白胆固醇水平显著高于对照组(P<0.05)。治疗后对照组血清miR-146a水平显著低于观察组(1.80±0.57 *vs* 2.25±0.66，t=4.895，P<0.01)，miR-351水平显著高于观察组(4.11±1.47 *vs* 3.50±1.54，t=2.718，P=0.007)。观察组总有效率为94.44%，显著高于对照组的82.22%(χ^2=6.523，P=0.011)。**结论**　司美格鲁肽治疗T2DM患者具有显著疗效，通过调节miR-146a与miR-351水平，恢复胰岛功能，进而降低血糖血脂，且安全性较高。

关键词：司美格鲁肽；2型糖尿病；二甲双胍；恩格列净；微小RNA；微小RNA-146a；微小RNA-351；胰岛功能

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Effects of semaglutide on islet function in patients with type 2 diabetes mellitus

ZHOU Yanling*, JIANG Hui, HONG Xin, TONG Deyin, CAO Shengkun

*Department of Pharmacy, Jiangsu Province (Suqian) Hospital, Suqian, Jiangsu 223800, China

Corresponding author: CAO Shengkun, E-mail: dvuamxa854@163.com

Abstract: Objective　To investigate the efficacy of semaglutide in treating patients with type 2 diabetes mellitus (T2DM) and its effects on islet function, serum microRNA(miR)-146a and miR-351. **Methods**　A total of 180 patients with T2DM admitted to Jiangsu Provincial (Suqian) Hospital from February 2023 to January 2024 were selected. They were randomly divided into a control group (n=90) and an observation group (n=90). The control group received metformin and empagliflozin tablets, while the observation group received the same treatment along with semaglutide for 90 days. Relevant indicators, such as blood glucose, blood lipids, islet function, miR-146a, and miR-351 levels, as well as therapeutic efficacy and adverse reactions, were measured and recorded before and after treatment. **Results**　After treatment, the observation group showed lower levels of blood glucose(fasting blood glucose, 2-hour postprandial blood glucose, and glycosylated hemoglobin), blood lipids (triglyceride, total cholesterol, low-density lipoprotein cholesterol), and islet function [fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR)] compared to the control group (P<0.05). The homeostasis model assessment of pancreatic β-cell function index, and high-density lipoprotein cholesterol levels in the observation group were significantly higher than those in the control group (P<0.05). After treatment, the serum level of miR-146a in the control group was significantly lower than that in the observation group (1.80±0.57 *vs* 2.25±0.66, t=4.895, P<0.01), and miR-351 levels were significantly higher than that in the observation group (4.11±1.47 *vs* 3.50±1.54, t=2.718, P=0.007). The total effective rate in the observation group was 94.44%, significantly higher than the 82.22% in the control group (χ^2=6.523, P=0.011). **Conclusion**　Semaglutide treatment shows significant efficacy in T2DM patients by regulating the levels of miR-146a and miR-351, restoring islet

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通信作者：曹胜焜，E-mail: dvuamxa854@163.com

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function, reducing blood glucose and lipids, and ensuring high safety.

Keywords: Semaglutide; Type 2 diabetes mellitus; Metformin; Empagliflozin; microRNA; miR-146a; miR-351; Islet function

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随着年龄的增长和代谢功能的下降，糖尿病的发病率逐渐上升，尤其在中老年群体中更为显著。这一群体因身体机能和代谢功能的减退，胰岛素分泌机制受到干扰，从而增加了患糖尿病的风险，其中2型糖尿病（type 2 diabetes mellitus，T2DM）占主导地位。据统计，T2DM占所有糖尿病类型的95%以上[1]，是糖尿病患者面临并发症风险和死亡率增加的主要原因[2]。T2DM的病理特征包括胰高血糖素样肽-1（glucagon-like peptide-1，GLP-1）水平低下、血脂代谢失衡及显著的胰岛素抵抗[3]，这些病理状态若得不到有效改善，将引发持续高血糖，进而促使动脉粥样硬化、糖尿病视网膜病变、糖尿病足和糖尿病周围神经病变等并发症的发生，严重影响患者生活质量与预后。司美格鲁肽作为一种GLP-1受体激动剂，近年来在降低血糖和控制体质量方面表现出显著效果[4]。随着分子生物学研究的深入，微小RNA（microRNA，miRNA）作为一类基因表达调控因子，在糖尿病及其并发症发展中的作用也日益受到关注。其中，miR-351在高脂诱导的糖尿病小鼠模型中特异性上调[5]，miR-146a在糖尿病视网膜病变患者中表达下调[6]。基于这些发现，推测血清中miR-351和miR-146a水平可能反映了T2DM的疾病状态，并在疾病进展中发挥重要作用。因此，本研究旨在探讨司美格鲁肽对T2DM患者的疗效，通过观察其对血清miR-351、miR-146a及胰岛功能的影响，以期为T2DM患者的治疗提供新的科学依据。

1 资料与方法

1.1 *一般资料* 选取2023年2月至2024年1月期间，江苏省人民医院宿迁医院收治的180例T2DM患者作为研究对象，通过随机分配的方式分为对照组（90例）和观察组（90例）。纳入标准：符合T2DM诊断标准[7]；年龄大于45岁；身体质量指数（body mass index，BMI）≥24 kg/m^2；临床资料完整。排除标准：对司美格鲁肽过敏；已有明显感染；处于心脑血管病急性期；伴有恶性肿瘤、血液系统、自身免疫系统疾病；妊娠期或哺乳期妇女。本研究已获得江苏省人民医院宿迁医院伦理委员会批准（伦审号：2024-SL-0182），研究对象均对本研究知情同意。两组患者年龄、性别、BMI和糖尿病病程差异均无统计学意义（P>0.05）。见表1。

1.2 *治疗方法* 对照组患者接受二甲双胍恩格列净片（杭州中美华东制药，国药准字H20213448，规格：每片含盐酸二甲双胍500 mg与恩格列净5 mg）治疗，进餐或餐后服用，1片/次，2次/d。观察组患者在接受上述治疗的基础上，联合司美格鲁肽（诺和诺德，国药准字SJ20210014，规格1.5 mg/mL）治疗，司美格鲁肽初始剂量0.25 mg/次，皮下注射给药，治疗4周后，改为0.5 mg/次，1次/周。两组患者均连续治疗90 d。

1.3 观察指标

1.3.1 *疗效评价标准*[8] 显效：临床症状和生命体征趋于正常，血糖下降到正常水平。有效：临床症状和生命体征有所改善，血糖水平显著降低。无效：糖尿病症状未见改善或有加重现象。总有效率=（显效例数+有效例数）/总例数×100%。

1.3.2 *血清miR-146a、miR-351因子检测* 分别于治疗前和治疗结束采集两组患者空腹静脉血5 mL。低温离心血液得到血清，分装并保存备用。采用Trizol法（美国Thermo Fisher Scientific公司）提取血清总RNA。采用逆转录试剂盒（美国Thermo Fisher Scientific公司）进行cDNA的逆转录，使用SYBR®Premix Ex Taq™试剂盒（日本Takara公司）进行qRT-PCR扩增。采用$2^{-\Delta\Delta Ct}$方法计算血清中miR-146a、miR-351相对表达量。miR-146a、miR-351和U6引物均由广州锐博生物科技有限公司合成。miR-146a正向序列5′-TGA GAA CTG AAT TCC ATG GGT T-3′，反向序列5′-GCT GTC AAC GAT ACG CTA CGT AAC G-3′。miR-351正向序列5′- ACA CTC CAG CTG GTC CCT GAG GAG CCC GG-3′，反向序列5′- CTC AAC TGG TGT CGT GGA GTC GGC AAT TCA GTT GAG TCA GGC TC-3′，U6正向序列5′-AAG GTG AAG CTG GGA GTC AAC-3′，反向序列为5′- GGG GTC ATT GAT GGC AAC AAT A-3′。

1.3.3 *血糖、血脂和胰岛功能检测* 分别于治疗前和治疗90 d采集对照组和观察组患者次日空腹血液5 mL。在3 000 r/min下离心（离心力为1 000×g），全自动生化检测仪（贝克曼库尔特DX800型）检测空腹血糖（fasting plasma glucose，FPG）、餐后2 h血糖

(2-hour postprandial blood glucose, 2hPG)、糖化血红蛋白(glycosylated hemoglobin, HbA1c)、三酰甘油(triglyceride, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)。采用全自动生化分析仪(罗氏 Cobas-6000 型)检测空腹胰岛素(fasting insulin, FINS)、稳态模型评估胰岛素抵抗指数(homeostasis model assessment of insulin resistance, HOMA-IR)、稳态模型评估胰岛β细胞功能指数(HOMA of pancreatic beta-cell function, HOMA-β)。

1.3.4　药物不良反应　在两组患者治疗期间,统计不良反应发生事件,主要包括恶心、腹泻、头痛和低血糖。

1.4　统计学方法　使用 SPSS 24.0 软件进行统计分析。分类变量采用例(%)表示,并使用 χ^2 检验分析。符合正态分布的连续变量以 $\bar{x}\pm s$ 表示,并使用 t 检验进行分析。P<0.05 为差异有统计学意义。

2　结　果

2.1　两组患者临床疗效评估　观察组总有效率为 94.44%,显著高于对照组的 82.22%,差异有统计学意义(P<0.05)。见表 2。

2.2　两组患者血糖水平比较　与对照组相比,观察组治疗后的 FPG、2hPG、HbA1c 均显著降低(P<0.05)。见表 3。

2.3　两组患者血脂水平比较　观察组治疗后的 TC、TG、LDL-C 均显著低于对照组,HDL-C 高于对照组(P<0.05)。见表 4。

2.4　两组患者胰岛功能指标比较　观察组治疗后的 HOMA-β显著高于对照组(P<0.05),FINS、HOMA-IR 显著低于对照组(P<0.05)。见表 5。

2.5　两组患者血清 miR-146a、miR-351 水平比较　观察组治疗后的 miR-146a 高于对照组(P<0.05),miR-351 低于对照组(P<0.05)。见表 6。

2.6　不良反应发生情况　对照组发生恶心 2 例,腹泻 1 例,头痛 2 例,低血糖 2 例。观察组发生恶心 2 例,头痛 1 例,低血糖 1 例。对照组和观察组的不良反应总发生率差异无统计学意义(7.78% *vs* 4.44%, χ^2=0.871, P=0.351)。

表 1　两组患者一般资料比较　(n=90, $\bar{x}\pm s$)

Tab.1　Comparison of general data between the two groups of patients　(n=90, $\bar{x}\pm s$)

组别	性别(男/女,例)	年龄(岁)	BMI(kg/m²)	糖尿病病程(年)
对照组	48/42	64.50±6.32	25.72±3.10	8.60±2.90
观察组	46/44	63.97±6.40	25.61±3.02	8.73±2.54
χ^2/t 值	0.089	0.559	0.241	0.320
P 值	0.765	0.577	0.810	0.749

表 2　两组患者疗效比较　[n=90,例(%)]

Tab.2　Comparison of treatment efficacy between the two groups of patients　[n=90, case(%)]

组别	无效	显效	有效	总有效率(%)
对照组	16(17.78)	45(50.00)	29(32.22)	82.22
观察组	5(5.56)	55(61.11)	30(33.33)	94.44
χ^2 值				6.523
P 值				0.011

表 3　两组患者治疗前后血糖指标比较　(n=90, $\bar{x}\pm s$)

Tab.3　Comparison of blood glucose indicators between two groups of patients before and after treatment　(n=90, $\bar{x}\pm s$)

组别	FPG(mmol/L)		2hPG(mmol/L)		HbA1c(%)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组	9.50±1.91	6.64±0.54[a]	13.50±2.65	8.31±0.69[a]	8.72±0.84	6.56±0.73[a]
观察组	9.42±1.86	6.20±0.70[a]	13.40±2.39	7.30±0.82[a]	8.66±0.93	5.58±0.69[a]
t 值	0.285	4.772	0.266	8.941	0.454	9.256
P 值	0.776	<0.001	0.791	<0.001	0.650	<0.001

注:相较于同组治疗前,[a]P<0.05。

表 4　两组患者血脂水平比较　(n=90, $\bar{x}\pm s$)

Tab.4　Comparison of blood lipid levels between two groups of patients　(n=90, $\bar{x}\pm s$)

组别	TC(mmol/L)		TG(mmol/L)		LDL-C(mmol/L)		HDL-C(mmol/L)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组	5.53±1.20	4.35±0.65[a]	3.15±0.90	1.76±0.82[a]	4.32±0.30	2.63±0.42[a]	1.18±0.26	1.31±0.25[a]
观察组	5.48±1.28	3.89±0.68[a]	3.10±0.94	1.20±0.76[a]	4.40±0.38	2.11±0.30[a]	1.15±0.23	1.50±0.28[a]
t 值	0.270	4.639	0.364	4.752	1.568	9.558	0.820	4.044
P 值	0.787	<0.001	0.716	<0.001	0.119	<0.001	0.413	<0.001

注:相较于同组治疗前,[a]P<0.05。

表5 两组患者胰岛功能指标比较 （n=90，$\bar{x}\pm s$）

Tab.5 Comparison of pancreatic islet function indicators between two groups of patients （n=90，$\bar{x}\pm s$）

组别	FINS(μIU/mL)		HOMA-IR		HOMA-β	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组	16.79±4.70	14.95±3.81[a]	5.20±1.19	4.16±1.01[a]	34.20±10.27	60.26±18.17[a]
观察组	17.06±4.85	12.89±3.30[a]	5.10±1.16	3.48±0.90[a]	34.50±10.19	73.32±20.15[a]
t值	0.379	3.169	0.571	4.769	0.197	4.566
P值	0.705	0.002	0.569	<0.001	0.844	<0.001

注：相较于同组治疗前，[a]P<0.05。

表6 两组患者治疗前后的miR-146a、miR-351水平比较（n=90，$\bar{x}\pm s$）

Tab.6 Comparison of miR-146a and miR-351 levels between two groups of patients before and after treatment （n=90，$\bar{x}\pm s$）

组别	miR-146a		miR-351	
	治疗前	治疗后	治疗前	治疗后
对照组	0.80±0.17	1.80±0.57[a]	6.31±2.01	4.11±1.47[a]
观察组	0.83±0.19	2.25±0.66[a]	6.35±1.90	3.50±1.54[a]
t值	1.116	4.895	0.137	2.718
P值	0.266	<0.001	0.891	0.007

注：相较于同组治疗前，[a]P<0.05。

3 讨 论

T2DM是由于胰岛素缺乏或胰岛素生物活性受损导致糖代谢紊乱，以长期高血糖为特征的代谢性疾病，常伴有多种代谢紊乱。T2DM早期症状并不表现典型的“三多一少”，因此，极易造成漏诊。有研究表明，全球T2DM患者数量的增加与超重、肥胖等因素有关，其机制可能是其自身的胰岛素抵抗[9]。目前临床上常用二甲双胍、恩格列净、利拉鲁肽等药物治疗[10]，但长期使用单一药物，会导致机体耐药性增加，治疗效果下降[11]。因此探索更为综合有效的药物对于治疗T2DM患者、改善其预后具有重要意义。司美格鲁肽作为肠道分泌的一种肠源性激素，是新型长效GLP-1类似物，其主要作用于胰岛β细胞，促进胰岛素的合成和分泌，减少肝糖释放，增强胰岛素敏感性，作用于下丘脑抑制食欲，并通过上述作用共同达到降糖的效果，对糖尿病具有良好的治疗效果[12]。相关研究也证实司美格鲁肽联合二甲双胍恩格列净片治疗T2DM患者具有显著疗效[13-14]。本研究也发现，司美格鲁肽联合二甲双胍恩格列净治疗T2DM患者总有效率显著高于二甲双胍恩格列净单用，且不良反应发生率差异无统计学意义。以上表明司美格鲁肽治疗T2DM患者具有较好的疗效，且治疗T2DM安全性高。

据有关研究揭示，GLP-1受体激动剂能够通过调节小肠上皮细胞的脂蛋白释放以及脂肪的分解，来降低TG、TC、LDL-C含量，这显示了司美格鲁肽具有间接调控血脂水平的能力[15]。张凤丽等[16]研究也证实司美格鲁肽具有降低血糖和血脂的功效。FINS、HOMA-IR和HOMA-β是医学上常用来评估胰岛功能的重要指标。HOMA-IR反映了机体的胰岛素抵抗水平，其指数越高，表明机体对胰岛素的敏感性越低，胰岛素抵抗程度越严重。HOMA-β则反映了胰岛β细胞的功能。胰岛β细胞是胰腺中分泌胰岛素的主要细胞，负责根据机体的血糖水平调节胰岛素的分泌。此外，也有研究揭示，司美格鲁肽联合二甲双胍恩格列净片在降低肥胖T2DM患者FPG、2hPG、HbA1c和HOMA-IR水平的同时，升高HOMA-β水平，提示司美格鲁肽可能通过恢复胰岛功能，降低血糖[17]。本研究发现，观察组FPG、2hPG、HbA1c和TC、TG、LDL-C、FINS、HOMA-IR水平显著低于对照组，而HDL-C、HOMA-β水平显著高于对照组，提示司美格鲁肽可能通过恢复胰岛功能，降低血糖和血脂水平，改善T2DM。

miRNA在T2DM的发生发展中具有重要作用。研究发现，miR-146a参与糖尿病的发展，其表达失调加快了糖尿病的进程[18]。miR-146a通过负性调控信号转导和免疫反应在各种生理过程中发挥作用。陈琳[19]在妊娠期糖尿病患者血清中观察到，与胰岛素抵抗组相比，极度、严重胰岛素抵抗组miR-146a水平显著降低，提示miR-146a可能与胰岛素抵抗相关。分析其原因：当miR-146a水平过低时，容易发生胰岛功能障碍，进而加重胰岛素抵抗。也有研究发现，miR-146a低表达还会促进炎症因子高表达，加剧机体炎症反应，造成高血糖和高血脂等慢性病的发生和发展[20]。另一方面，miR-351也被发现与糖尿病及其并发症密切相关。Badacz等[21]研究揭示，miR-351可以通过靶向调控与糖脂代谢相关基因和信号通路（如AMPK、PPARγ等），影响糖脂合成、分解和运输等过程，这表明miR-351可能与脂质合成相关。研究指出，miR-351通过负调节糖脂代谢、促进炎症反应和细胞凋亡，进而调控颈动脉粥样硬化的发展[22]。此外，动物

实验表明，在糖尿病小鼠的转录组中，高脂质诱导的糖尿病小鼠体内的 miR-351 特异性上调，提示 miR-351 的上调可能在糖尿病和动脉粥样硬化的进展中起到促进的作用[22]。本研究发现，治疗后观察组 miR-146a 水平显著高于对照组，而 miR-351 水平显著低于对照组，提示司美格鲁肽可能通过调节 miR-146a、miR-351 水平，促进胰岛功能恢复，进而减少糖脂分泌，改善胰岛素抵抗。

综上所述，司美格鲁肽联合二甲双胍恩格列净片治疗 T2DM 具有显著疗效，可能通过调节 miR-146a、miR-351 异常表达，改善胰岛功能，减轻胰岛素抵抗，进而降低血糖、血脂水平。但本研究也有不足之处，样本数量相对较小，后续应扩大样本量。司美格鲁肽治疗 T2DM 的具体机制尚需进一步探讨。未来研究可关注司美格鲁肽对 miRNA 的调控作用以及其对胰岛功能的长期影响，以期为 T2DM 的治疗提供更全面的依据。

利益冲突　无

参考文献

[1] Yoon HS, Cho CH, Yun MS, et al. Akkermansia muciniphila secretes a glucagon-like peptide-1-inducing protein that improves glucose homeostasis and ameliorates metabolic disease in mice[J]. Nat Microbiol, 2021, 6(5):563-573.

[2] Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: a comparative risk assessment[J]. Lancet Diabetes Endocrinol, 2014, 2(8):634-647.

[3] Nolen-Doerr E, Stockman MC, Rizo I. Mechanism of glucagon-like peptide 1 improvements in type 2 diabetes mellitus and obesity[J]. Curr Obes Rep, 2019, 8(3):284-291.

[4] 卢伟涛，何家汝，陈文瑛. 基于FAERS数据库的司美格鲁肽药品不良事件信号挖掘[J]. 中国药房，2022，33(15)：1865-1869，1875.

[5] Li HP, Fan JH, Zhao YR, et al. Nuclear miR-320 mediates diabetes-induced cardiac dysfunction by activating transcription of fatty acid metabolic genes to cause lipotoxicity in the heart[J]. Circ Res, 2019, 125(12):1106-1120.

[6] Chen SD, Yuan ME, Liu YM, et al. Landscape of microRNA in the aqueous humour of proliferative diabetic retinopathy as assessed by next-generation sequencing[J]. Clin Exp Ophthalmol, 2019, 47(7):925-936.

[7] 中华医学会糖尿病学分会.中国2型糖尿病防治指南(2020年版)[J].中华糖尿病杂志，2021，13(4)：315-409.

[8] 关子安.现代糖尿病学[M].天津：天津科学技术出版社，2020：461-465.

[9] Chilunga FP, Henneman P, Meeks KA, et al. Prevalence and determinants of type 2 diabetes among lean African migrants and non-migrants: the RODAM study[J]. J Glob Health, 2019, 9(2):020426.

[10] 景昱，石洁，鹿斌，等. 2型糖尿病患者血清脂质运载蛋白2水平与心血管疾病的相关性研究[J]. 中华内分泌代谢杂志，2021，37(4)：267-273.

[11] 叶娟，陈冬，邱振汉，等. 司美格鲁肽联合达格列净、二甲双胍在肥胖型2型糖尿病合并非酒精性脂肪肝患者中的疗效分析[J]. 糖尿病新世界，2024，27(1)：19-22.

[12] 甘秀军，詹玲球. 超早期康复护理干预对老年缺血性脑卒中患者肢体功能恢复和生活质量的影响[J]. 吉林医学，2023，44(4)：1134-1137.

[13] 徐启超，覃平柔，徐冬梅. 司美格鲁肽联合达格列净对二甲双胍治疗不佳的2型糖尿病患者的影响[J]. 中国医学创新，2024，21(27)：70-75.

[14] 王艳，涂振兴，廖华萍，等. 司美格鲁肽联合恩格列净与二甲双胍治疗初诊肥胖2型糖尿病患者的临床效果[J]. 临床合理用药，2024，17(27)：18-21.

[15] Okamoto A, Yokokawa H, Nagamine T, et al. Efficacy and safety of semaglutide in glycemic control, body weight management, lipid profiles and other biomarkers among obese type 2 diabetes patients initiated or switched to semaglutide from other GLP-1 receptor agonists[J]. J Diabetes Metab Disord, 2021, 20(2):2121-2128.

[16] 张凤丽，张东凤，赵一楠，等. 司美格鲁肽对2型糖尿病患者心血管危险因素的影响[J]. 中国医药，2022，17(12)：1800-1803.

[17] 逯海波，马瑜瑾，李利平，等. 司美格鲁肽联合达格列净、二甲双胍在肥胖型糖尿病患者中的疗效分析[J]. 临床研究，2024，32(10)：73-76.

[18] 杨开雯，强郑，靳贝芳，等. microRNA-146在糖尿病心肌病中的调控作用[J]. 中国病理生理杂志，2018，34(11)：1947-1952.

[19] 陈琳. 妊娠期糖尿病患者血清miR-146a表达与胰岛素抵抗的关系[J]. 实用医技杂志，2022，29(3)：279-282，337.

[20] Fumimoto C, Yamauchi N, Minagawa E, et al. miR-146a is mutually regulated by high glucose-induced oxidative stress in human periodontal ligament cells[J]. Int J Mol Sci, 2024, 25(19):10702.

[21] Badacz R, Przewłocki T, Legutko J, et al. microRNAs associated with carotid plaque development and vulnerability: the clinician's perspective[J]. Int J Mol Sci, 2022, 23(24):15645.

[22] 韩琦，朱伟，王晓慧，等. miR-638在糖尿病肾病中的研究进展[J]. 华南国防医学杂志，2020，34(8)：591-593.

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