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Short-term continuous subcutaneous insulin infusion combined with metformin and semaglutide in the treatment of type 2 diabetes mellitus

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Abstract: **Objective** To observe the effect of short-term continuous subcutaneous insulin infusion (CSII)combined with metformin and semaglutide in the remission of type 2 diabetes mellitus (T2DM), glycolipid metabolism, islet β cell function, and weight. **Methods** A total of 42 T2DM patients from the Department of Endocrinology at Geriatric Hospital of Nanjing Medical University were enrolled from September 2022 to December 2023. These patients were given 7-day CSII for intensive therapy during hospitalization, then combined with metformin and semaglutide, and were followed up for 48 weeks. The rate of diabetes remission was calculated. Changes of glycolipid metabolism indicators, islet β cell function, and body mass were compared between remission group and non-remission group. **Results** After short-term treatment with CSII combined with metformin and semaglutide, the remission rate of T2DM was 54.76% at the 48th of follow-up. Compared with non-remission group, remission group showed more significant improvements in fasting blood glucose, glycated hemoglobin (HbA1C), and glycated albumin at the 12th, 24th, and 36th weeks of follow- up (P<0.05), and the Disposal Index significantly increased at the 12th week (P<0.05). During the follow-up period, body mass and waist circumference decreased significantly (P<0.05), and high density lipoprotein cholesterol increased significantly (P<0.05). Univariate logistic regression analysis revealed that baseline 2-hour postprandial blood glucose (OR=1.204, 95% CI: 1.003- 1.446) and medication duration (OR=0.386, 95% CI: 0.229- 0.650) were influencing factors for remission of T2DM (P<0.05). **Conclusion** Short - term CSII combined with metformin and semaglutide can achieve higher rate of T2DM remission. Combination therapy can correct glycolipid metabolism dysfunction, improve islet β cell function and reduce body weight.

Keywords: Insulin intensive therapy; Type 2 diabetes mellitus; Diabetes remission; Metformin; Semaglutide; Continuous subcutaneous insulin infusion; Glycolipid metabolism; Glucose disposal rate

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Studies have confirmed that hyperglycemia can be reversed in some patients with type 2 diabetes mellitus (T2DM) after intervention, thereby achieving diabetes remission [1]. Continuous subcutaneous insulin infusion (CSII) has been recommended as the preferred regimen for diabetes reversal therapy [2]. The SUSTAIN series of studies found that glycated hemoglobin (HbA1c) was significantly reduced after semaglutide treatment, and some patients achieved normalization of blood glucose [3], suggesting its potential to induce diabetes remission. This study observed changes in diabetes remission, glycolipid metabolism, and body weight in patients with T2DM after short-term CSII combined with metformin and semaglutide, aiming to provide a new clinical strategy for diabetes remission therapy.

1. Subjects and Methods

1.1 Study Subjects

Forty-two patients with T2DM hospitalized in the Department of Endocrinology, Geriatric Hospital Affiliated to Nanjing Medical University, from September 2022 to December 2023 were selected as study subjects.

Inclusion criteria: (1) Age >18 years. **(2)** HbA1c ≥7.5%. **(3)** Duration of diabetes <5 years. **(4)** No glucose-lowering medication or metformin only. **(5)** Body mass index (BMI) ≥18.5 kg/m².

Exclusion criteria: (1) Type 1 diabetes mellitus, latent autoimmune diabetes in adults, or secondary diabetes mellitus. **(2)** Acute diabetic complications or severe chronic complications. **(3)** Any type of anemia affecting HbA1c levels. **(4)** Fasting C-peptide <1.2 ng/mL. **(5)** Severe cardiac, hepatic, or renal disease. **(6)** Uncontrolled severe infectious disease. **(7)** Use of drugs affecting blood glucose, such as glucocorticoids or antipsychotics. **(8)** Cognitive impairment or inability to cooperate with the study and follow-up. **(9)** Malignant tumors or other diseases with expected survival <5 years.

This study was approved by the Ethics Committee of Geriatric Hospital Affiliated to Nanjing Medical University (approval No. 2022-019-3), and all participants signed informed consent.

1.2 Study Methods

General information, including age, duration of diabetes, height, and body weight, was collected, and BMI was calculated. All enrolled patients received lifestyle guidance, including individualized dietary and exercise recommendations. After admission, patients received short-term intensive treatment with CSII via an insulin pump for 7 days. After contraindications were excluded, patients received oral metformin hydrochloride tablets (Sino-American Shanghai Squibb Pharmaceuticals,

approval No. H20023370; 0.5 g per dose, 2-3 times daily) combined with subcutaneous semaglutide injection (Novo Nordisk, Denmark; approval Nos. SJ20210014, 1.34 mg/mL, 1.5 mL; SJ20210015, 1.34 mg/mL, 3 mL). The initial dose of semaglutide was 0.25 mg once weekly, adjusted to 0.5 mg once weekly after 4 weeks, with a maximum dose of 1.0 mg once weekly.

After discharge, patients monitored blood glucose at home. A telephone follow-up was conducted at week 2 to assess regimen adherence and adverse drug reactions. Patients with severe intolerable gastrointestinal reactions were excluded from efficacy analysis. Thereafter, telephone follow-up was performed monthly to collect fasting blood glucose (FBG) and 2-hour postprandial blood glucose (2hPBG), and dietary and exercise guidance was reinforced. Patients returned to the outpatient clinic every 12 weeks after discharge for oral glucose tolerance test (OGTT), blood biochemistry, and lipid testing. Waist circumference, BMI, HbA1c, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), estimated glomerular filtration rate (eGFR), and disposition index (DI) were recorded. Patients who met the criteria for medication withdrawal discontinued medication and were observed. They were instructed to continue lifestyle intervention and were reassessed in the outpatient clinic 12 weeks later to determine whether remission criteria had been met. Patients whose FBG exceeded the hyperglycemia threshold were required to return to the hospital for treatment. Follow-up ended after 48 weeks. The criteria for medication withdrawal were FBG ≤6.0 mmol/L and 2hPBG ≤8.0 mmol/L. Diabetes remission was defined as HbA1c <6.5% after withdrawal of glucose-lowering medication for at least 3 months, or FBG <7.0 mmol/L as an alternative criterion [4]. Patients who met remission criteria after medication withdrawal were assigned to the remission group. Patients who did not discontinue medication within 48 weeks or did not meet remission criteria after discontinuation were assigned to the non-remission group. Changes in glycolipid metabolism, pancreatic β-cell function (DI), waist circumference, BMI, and body weight were compared between the two groups.

1.3 Statistical Analysis

SPSS 27.0 was used for statistical analysis. Normally distributed continuous variables are expressed as $\bar{x}\pm s$, and within-group comparisons were performed using the t test. Comparisons across multiple time points were performed using repeated-measures analysis of variance, with LSD-*t* test for pairwise comparisons. Non-normally distributed continuous variables are expressed as M (Q_1, Q_3). Between-group comparisons were performed using the rank-sum test. Repeated-measures data were analyzed using the Brunner nonparametric model for group effects, time effects, and group-by-time interaction effects. If an effect was significant, Bonferroni-corrected paired Wilcoxon signed-rank tests were used for pairwise comparisons. Categorical data are expressed as cases (%). Between-group comparisons were performed using the χ^2 test. Within-group comparisons across multiple time points were performed using Cochran's Q test, and pairwise comparisons were performed using the McNemar test with Bonferroni correction. Univariate logistic regression analysis was used to identify factors associated with diabetes remission. P<0.05 was considered statistically significant.

2. Results

2.1 Baseline Characteristics

According to follow-up outcomes, 23 patients were included in the remission group and 19 in the non-remission group, with a remission rate of 54.76%. Baseline 2hPBG and BMI were significantly higher in the remission group than in the non-remission group (P<0.05). No significant differences were observed in other baseline characteristics (P>0.05). See **Table 1**.

2.2 Comparison of Glucose Metabolism

FBG, HbA1c, and glycated albumin showed significant time effects in both groups (P<0.05), and FBG showed a significant interaction effect (P<0.05). During follow-up, glucose metabolism indicators improved significantly from baseline in both groups (P<0.05). At weeks 12, 24, and 36, glucose metabolism indicators in the remission group were significantly better than those in the non-remission group at the same time points (P<0.05). See **Table 2**.

2.3 Comparison of Body Weight and Waist Circumference

Changes in body weight and waist circumference showed significant group and interaction effects (P<0.05). During follow-up, reductions in body weight and waist circumference were more pronounced in the remission group than in the non-remission group (P<0.05). BMI change showed a significant time effect in both groups (P<0.05). BMI decreased more significantly in the remission group than in the non-remission group at weeks 12 and 48 (P<0.05). See **Table 3**.

2.4 Comparison of Lipid Indicators

Total cholesterol change showed a significant time effect (P<0.05). Total cholesterol decreased more significantly in the remission group than in the non-remission group at weeks 12 and 36 (P<0.05). HDL-C change showed significant group, time, and interaction effects (P<0.05). During follow-up, HDL-C increased significantly more in the remission group than in the non-remission group (P<0.05). See **Table 4**.

2.5 Comparison of Pancreatic β-Cell Function

DI showed significant time and interaction effects in both groups (P<0.05). During follow-up, DI increased significantly from baseline in both groups (P<0.05), and DI at week 12 was significantly higher in the remission group than in the non-remission group at the same time point (P<0.05). See **Table 5**.

2.6 Factors Associated with T2DM Remission

Indicators with statistically significant differences at baseline between the remission and non-remission groups, including BMI and 2hPBG, together with medication duration, were further included in univariate logistic regression analysis. The results showed that medication duration and baseline 2hPBG were factors associated with T2DM remission (P<0.05).

Table 1. Baseline characteristics between remission group and non-remission group

Clinical characteristic	Remission group (n=23)	Non-remission group (n=19)	$t/\chi^2/Z$ value	P value
Age, years	52.52±12.00	57.00±12.44	1.401	0.244
Sex, male/female	12/11	9/10	0.096	0.757
Duration of diabetes, months	3.00 (0.33, 24.00)	3.00 (1.00, 36.00)	0.482	0.630
History of metformin use, n (%)	8 (34.78)	8 (42.11)	0.237	0.627
Body weight, kg	77.00 (66.00, 84.00)	70.00 (64.00, 75.00)	1.555	0.120
Waist circumference, cm	94.13±10.72	90.05±8.82	1.762	0.192
BMI, kg/m²	26.80 (24.39, 29.41)	24.70 (22.68, 26.03)	2.009	0.045
SBP, mmHg	136.39±15.31	134.26±14.70	0.208	0.651
DBP mmHg	82.61±9.40	80.32±11.52	0.505	0.481
FBG at admission, mmol/L	9.05±3.18	8.58±3.58	0.200	0.657
2hPBG, mmol/L	14.93±4.57	12.29±2.97	4.711	0.036
HbA1c, %	9.74±1.99	9.46±1.91	0.214	0.646
Glycated albumin, %	23.39±10.07	21.76±5.50	0.399	0.531
Total cholesterol, mmol/L	4.64±1.39	5.00±1.25	0.789	0.380
Triglycerides, mmol/L	1.88±1.13	1.56±0.63	1.206	0.279
LDL-C, mmol/L	2.79±0.99	3.00±0.88	0.531	0.470
HDL-C, mmol/L	1.01±0.28	1.09±0.19	1.044	0.313
ALT, U/L	32.00 (17.00, 47.00)	21.00 (14.00, 42.00)	0.657	0.511
AST, U/L	21.00 (14.00, 32.00)	19.00 (14.00, 28.00)	0.569	0.569
GGT, U/L	35.00 (25.00, 48.00)	26.00 (19.00, 50.00)	0.582	0.561
SUA, μmol/L	337.00 (258.00, 378.00)	286.00 (269.00, 339.00)	1.036	0.300
Serum creatinine, μmol/L	64.13±15.65	57.36±20.11	1.507	0.227
eGFR, mL/(min·1.73 m²)	104.20±16.47	103.09±17.84	0.044	0.834

Table 2. Comparison of glucose metabolism indicators between remission group and non-remission group ($\bar{x}\pm s$)

Time-point	FBG (mmol/L)		HbA1c (%)		Glycated Albumin (%)	
	Remission group (n=23)	Non-remission group (n=19)	Remission group (n=23)	Non-remission group (n=19)	Remission group (n=23)	Non-remission group (n=19)
Baseline	8.47±2.88	7.64±1.56	9.74±1.99	9.46±1.91	23.39±10.07	21.76±5.50
12 weeks	5.57±0.53[ab]	6.46±0.91[a]	5.88±0.46[ab]	6.41±0.40[a]	12.19±1.98[ab]	14.18±3.72[a]
24 weeks	5.65±0.58[ab]	6.22±0.78[a]	5.70±0.43[ab]	6.26±0.40[a]	12.87±1.71[ab]	14.32±1.78[a]
36 weeks	5.88±0.82[ab]	6.39±0.77[a]	5.93±0.41[ab]	6.41±0.46[a]	13.17±1.38[ab]	14.42±1.99[a]
48 weeks	6.22±1.06[a]	6.67±0.87[a]	6.23±0.70[a]	6.60±0.60[a]	13.49±2.04[a]	14.53±1.39[a]
$F_{group}/F_{time}/F_{interaction}$	1.937/23.225/4.869		4.302/84.256/3.789		0.369/72.015/2.655	
$P_{group}/P_{time}/P_{interaction}$	0.181/<0.001/0.041		0.053/<0.001/0.067		0.551/<0.001/0.120	

Notes: Compared with the baseline of the same group, [a]P<0.05; compared with the non-remission group at the same time point, [b]P<0.05.

Table 3. Comparison of weight and waist circumference between remission group and non-remission group [M (Q_1, Q_3)]

Time-point	Body mass difference (kg)		Waist circumference difference (cm)		BMI difference (kg/m²)	
	Remission group (n=23)	Non-remission group (n=19)	Remission group (n=23)	Non-remission group (n=19)	Remission group (n=23)	Non-remission group (n=19)
12 weeks	-4.00(-7.00,-2.90)[a]	-3.30(-5.00,2.00)	-6.00(-9.00,-3.00)[a]	-1.00(-2.00,0)	-1.70(-2.44,-1.10)[a]	-0.95(-1.65,0.96)
24 weeks	-4.80(-7.30,-3.00)[a]	-4.00(-7.50,0.10)	-7.00(-11.00,-3.00)[a]	-2.00(-5.00,3.00)	-1.80(-2.74,-1.31)	-1.27(-2.40,-0.14)
36 weeks	-4.10(-7.00,-2.40)[a]	-4.20(-5.40,0.30)	-3.00(-8.00,-2.00)[a]	-3.00(-9.00,-1.00)	-1.70(-2.30,-0.87)	-1.42(-1.83,0.06)
48 weeks	-4.80(-7.10,-2.00)[a]	-0.10(-4.10,0.30)	-7.50(-10.00,0)[a]	-2.00(-6.00,12.00)	-1.63(-2.40,-0.18)[a]	-0.42(-1.50,0.28)
W_{group} / W_{time} /$W_{interaction}$	17.856/2.235/6.920		4.998/1.818/9.987		2.476/4.757/3.156	
P_{group} /P_{time}/$P_{interaction}$	<0.001/0.525/0.008		0.025/0.177/0.016		0.116/0.029/0.076	

Note: Compared with the non-remission group at the same time point, [a]P<0.05.

Table 4. Comparison of lipid indicators between remission group and non-remission group [M (Q_1, Q_3)]

Time-point	Total Cholesterol Difference (mmol/L)		HDL-C Difference (mmol/L)	
	Remission Group (n=23)	Non-Remission Group (n=19)	Remission Group (n=23)	Non-Remission Group (n=19)
12 Weeks	-0.80(-1.94,0.11)[a]	-0.79(-2.23,0)	0.11(-0.08,0.29)[a]	0.02(-0.16,0.20)
24 Weeks	-0.06(-1.63,0.22)	-0.55(-1.83,-0.13)	0.22(-0.02,0.35)[a]	0.17(-0.07,0.23)
36 Weeks	-0.47(-1.22,0.72)[a]	-0.58(-1.57,0.43)	0.32(0.08,0.54)[a]	0.01(-0.07,0.28)
48 Weeks	-0.40(-1.22,2.14)	-0.28(-1.38,0.45)	0.25(0.00,0.68)[a]	0.02(-0.11,0.27)
W_{group} / W_{time} /$W_{interaction}$	0.002/18.457/2.171		4.272/24.363/7.067	
P_{group} /P_{time}/$P_{interaction}$	0.964/<0.001/0.141		0.039/<0.001/0.008	

Table 5. Comparison of DI between remission group and non-remission group

Time Point	Remission Group (n=23)	Non-Remission Group (n=19)
Baseline	0.18(0.01,0.36)	0.28(0.15,0.66)
12 Weeks	0.57(0.42,0.86)[a]	0.39(0.21,0.51)[a]
24 Weeks	0.78(0.43,1.08)[a]	0.44(0.29,0.74)[a]
36 Weeks	0.52(0.42,0.88)[a]	0.47(0.31,0.73)[a]
48 Weeks	0.50(0.35,0.91)[a]	0.39(0.26,0.65)[a]
W_{group} / W_{time} /$W_{interaction}$	2.577/23.863/9.327	
P_{group} /P_{time}/$P_{interaction}$	0.108/<0.001/0.002	

3. Discussion

According to the International Diabetes Federation, China has the largest number of patients with diabetes worldwide [5]. In 2024, the prevalence of diabetes among adults in China was 11.9% [6], and China is expected to remain the country with the largest number of patients with diabetes by 2050. Diabetes prevention and control in China remains challenging. Early screening, timely intervention, glycemic control to target, and even early remission are particularly important.

Metformin is the first-line preferred medication for T2DM and the foundation of combination therapy. Intensive insulin therapy is an important approach for intensive glycemic control. Its core mechanism is to rapidly correct hyperglycemia by supplementing exogenous insulin, reduce glucotoxicity, lower inflammatory factor levels in the body [7], and improve chronic inflammation. It can significantly reduce the risk of macrovascular events and myocardial infarction, thereby improving prognosis [8]. At the same time, intensive insulin therapy can protect pancreatic β cells and promote restoration of β-cell function, significantly improving insulin secretory capacity and insulin sensitivity in target organs [9]. After 2-3 weeks of intensive insulin therapy, abnormal first-phase insulin secretion can be corrected [10], and blood glucose can remain at satisfactory levels for an extended period after treatment. Semaglutide promotes insulin secretion by pancreatic β cells in a glucose concentration-dependent manner while inhibiting glucagon secretion. It effectively improves fasting and postprandial blood glucose, significantly reduces HbA1c, lowers glycemic variability, and reduces the risk of hypoglycemic events, thereby achieving long-term stable glycemic regulation [3]. In addition, semaglutide reduces appetite, increases satiety, delays gastric emptying, reduces food absorption, and promotes weight loss by inhibiting the hypothalamic feeding center [11]. Related studies have confirmed that semaglutide significantly reduces the risk of major adverse cardiovascular events in patients with T2DM by improving lipid metabolism and reducing levels of proteins associated with atherosclerosis [12].

Previous studies have shown that after 4 weeks of liraglutide combined with insulin glargine and 12 weeks of insulin glargine combined with lixisenatide and metformin, remission rates of T2DM at week 48 were 42.74% and 22.8%, respectively [9,13]. In the present study, the remission rate of T2DM at week 48 reached 54.76%. This may be due to the synergistic effects of the mechanisms of the drugs in the combination regimen. Short-term intensive insulin therapy can correct hyperglycemia, relieve glucotoxic suppression of pancreatic β cells, and restore impaired secretory function [9]. Metformin enhances glucose-lowering effects by delaying glucose absorption, inhibiting hepatic glycogen output, and improving insulin sensitivity in peripheral tissues [14]. Semaglutide enhances glycemic regulation by promoting pancreatic β-cell secretion and inhibiting glucagon release [15], and further improves insulin resistance through significant weight reduction [11], thereby increasing insulin sensitivity in target organs. These mechanisms together produce a synergistic therapeutic effect.

The Chinese Expert Consensus on Remission of Type 2 Diabetes proposes the “ABCD” principle to predict the likelihood of diabetes remission, where “A” refers to insulin autoantibodies, “B” to BMI, “C” to C-peptide, and “D” to disease duration [16]. Other studies have also found that baseline HbA1c is associated with T2DM remission [17]. In this study, baseline BMI was higher in the remission group than in the non-remission group, consistent with the prediction principle, whereas disease duration and baseline HbA1c showed no statistically significant differences.

Univariate logistic regression analysis in this study showed that baseline 2hPBG and medication duration were factors associated with T2DM remission. Markedly elevated blood glucose can impair pancreatic β-cell secretory function. In this study, baseline 2hPBG was significantly higher and baseline DI was lower in the remission group than in the non-remission group, suggesting more severe impairment of β-cell function at baseline in the remission group. However, DI increased significantly from baseline in the remission group, indicating marked improvement in β-cell function. This may be because pancreatic β cells in the remission group had been exposed to hyperglycemia for a relatively short period and had not yet developed irreversible damage. Therefore, after treatment with the combination regimen, impaired β-cell secretory function was repaired in time, increasing the likelihood of remission. Medication duration was also an important factor affecting T2DM remission. At each follow-up time point, DI increased from baseline in both groups, indicating that prolonged medication duration may continuously improve β-cell function and consolidate the therapeutic effect of the combination regimen, thereby increasing the remission rate of T2DM. However, further multivariate regression analysis did not show statistically significant differences, and results remained nonsignificant after adjusting for confounding factors. This may be related to the limited sample size of only 42 patients, resulting in insufficient statistical power of the multivariate model. Therefore, the results of univariate regression analysis were ultimately adopted, and the associations of baseline 2hPBG and medication duration with T2DM remission need to be verified in larger populations.

Patients with diabetes have a significantly higher risk of atherosclerotic cardiovascular disease than individuals without diabetes [18]. Low HDL-C level is an independent risk factor for atherosclerotic cardiovascular disease, while higher LDL-C levels are associated with increased all-cause and cardiovascular mortality [19]. In this study, HDL-C increased from baseline after combination therapy, indicating that this regimen has certain efficacy in lipid management among patients with diabetes.

In this study, significant differences between the two groups mainly appeared at weeks 12 and 24. This may be due to the sustained effects of the combination regimen on blood glucose and body weight, as well as asynchronous medication withdrawal among patients in the remission group. Compared with the non-remission group, some patients in the remission group may already have discontinued medication for more than 12 weeks at the same time point. Their indicators may have rebounded with longer drug discontinuation, resulting in nonsignificant differences in some indicators between the two groups.

In conclusion, short-term CSII combined with metformin and semaglutide can significantly reduce blood glucose, body weight, and lipids, and achieve a higher proportion of diabetes remission. This study also has limitations. First, it was a small-sample, single-arm, self-controlled study, and the findings need to be further verified in larger randomized controlled trials. Second, due to time limitations, long-term remission and recurrence were not further observed. Future studies should extend follow-up to evaluate the long-term efficacy of this combination regimen.

Conflict of Interest None

Reference

[1] Liu Yuejun, Chen Ying, Ma Jianhua, et al. Dapagliflozin plus calorie restriction for remission of type 2 diabetes: multicentre, double blind, randomised, placebo controlled trial[J]. BMJ, 2025, 388: e081820.

[2] Chinese Insulin Secretion Study Group. Consensus statement on reversal of type 2 diabetes using short-term intensive insulin therapy[J]. Chin J Diabetes Mellit, 2021, 13(10): 949-959. **[In Chinese]**

[3] Kellerer M, Kaltoft M S, Lawson J, et al. Effect of once-weekly semaglutide versus thrice-daily insulin aspart, both as add-on to metformin and optimized insulin glargine treatment in participants with type 2 diabetes (SUSTAIN 11): a randomized, open-label, multinational, phase 3b trial[J]. Diabetes Obes Metab, 2022, 24(9): 1788-1799.

[4] Riddle M C, Cefalu W T, Evans P H, et al. Consensus report: definition and interpretation of remission in type 2 diabetes[J]. Diabetologia, 2021, 64(11): 2359-2366.

[5] SONG Xiaogang, CHEN Ziyi, MA Xia, et al, . Progress in role of lipotoxicity in pathogenesis of diabetic cardiomyopathy[J]. Chin J Pathophysiol, 2022, 38(11): : 2106-2112. **[In Chinese]**

[6] Chinese Diabetes Society, Chinese Medical Association.Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020 edition)[J]. Chin J Endocrinol Metab, 2021, 37(4): 311-398. **[In Chinese]**

[7] Esser N, Utzschneider K M, Kahn S E. Early beta cell dysfunction vs insulin hypersecretion as the primary event in the pathogenesis of dysglycaemia[J]. Diabetologia, 2020, 63(10): 2007-2021.

[8] Luo Sihui, Zheng Xueying, Bao Wei, et al. Real-world effectiveness of early insulin therapy on the incidence of cardiovascular events in newly diagnosed type 2 diabetes[J]. Sig Transduct Target Ther, 2024, 9: 154.

[9] McInnes N, Hall S, Hramiak I, et al. Remission of type 2 diabetes following a short-term intensive intervention with insulin glargine, sitagliptin, and metformin: results of an open-label randomized parallel-design trial[J]. Diabetes Care, 2022, 45(1): 178-185.

[10] Liu Liehua, Ke Weijian, Li Hai, et al. Intense simplified strategy for newly diagnosed type 2 diabetes in patients with severe hyperglycaemia: multicentre, open label, randomised trial[J]. BMJ, 2024, 387: e080122.

[11] Wang Shaoxin, Han Liping. Research progress on the weight loss effect of semaglutide[J]. Chin J Diabetes Mellit, 2024, 16(S2): 266-269. **[In Chinese]**

[12] Nauck M A, Quast D R. Cardiovascular safety and benefits of semaglutide in patients with type 2 diabetes: findings from SUSTAIN 6 and PIONEER 6[J]. Front Endocrinol, 2021, 12: 645566.

[13] Zhuo Yafen, Sun Zhichun, Hong Zhenzhen, et al. Effect of Liraglutide combine with insulin glargine in long-term clinical remission in newly diagnosed type 2 diabetes mellitus[J]. Chin J Diabetes, 2021, 29(10): 733-737. **[In Chinese]**

[14] Rena G, Hardie D G, Pearson E R. The mechanisms of action of metformin[J]. Diabetologia, 2017, 60(9): 1577-1585.

[15] Papakonstantinou I, Tsioufis K, Katsi V. Spotlight on the mechanism of action of semaglutide[J]. Curr Issues Mol Biol, 2024, 46(12): 14514-14541.

[16] Expert Writing Committee.Consensus of Chinese experts on the remission of type 2 diabetes mellitus[J]. Chin Gen Pract, 2021, 24(32): 4037-4048. **[In Chinese]**

[17] Holman N, Wild S H, Khunti K, et al. Incidence and characteristics of remission of type 2 diabetes in England: a cohort study using the national diabetes audit[J]. Diabetes Care, 2022, 45(5): 1151-1161.

[18] Xiao Yang, Yu Bilian, Chao Chen, et al. Chinese expert consensus on blood lipid management in patients with diabetes (2024 edition)[J]. J Transl Int Med, 2024, 12(4): 325-343.

[19] Joint Expert Committee, Wang Zengwu, Li Jianjun, et al. Chinese guideline for lipid management(primary care version 2024)[J]. Chin Gen Pract, 2024, 27(20): 2429-2436.**[In Chinese]**

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·论　著·

短期持续皮下胰岛素输注联合二甲双胍与司美格鲁肽治疗2型糖尿病

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摘要：目的　观察2型糖尿病（T2DM）患者经短期持续皮下胰岛素输注（CSII）联合二甲双胍与司美格鲁肽治疗后糖尿病缓解、糖脂代谢、胰岛β细胞功能及体质量变化。**方法**　选取2022年9月至2023年12月于南京医科大学附属老年医院内分泌科42例T2DM患者进行7天CSII治疗后联合使用二甲双胍与司美格鲁肽，并进行48周纵向随访，计算随访期间糖尿病缓解率，比较缓解组与未缓解组糖脂代谢、胰岛β细胞功能及体质量变化。**结果**　经短期CSII联合二甲双胍与司美格鲁肽治疗，随访第48周时T2DM缓解率达54.76%。与未缓解组相比，缓解组随访第12周、24周、36周时空腹血糖、糖化血红蛋白（HbA_{1C}）、糖化白蛋白改善更显著（$P<0.05$）、第12周葡萄糖处置指数显著升高（$P<0.05$），随访期间体质量、腰围显著下降（$P<0.05$），高密度脂蛋白胆固醇显著升高（$P<0.05$）。单因素logistic回归分析发现基线餐后2小时血糖（$OR=1.204$，95%CI：1.003~1.446）及用药时长（$OR=0.386$，95%CI：0.229~0.650）是T2DM缓解的影响因素（$P<0.05$）。**结论**　短期CSII联合二甲双胍与司美格鲁肽可实现更高比例的T2DM缓解，联合方案可纠正患者糖脂代谢异常、改善胰岛β细胞功能并减轻体质量。

关键词：胰岛素强化治疗；2型糖尿病；糖尿病缓解；二甲双胍；司美格鲁肽；持续皮下胰岛素输注；糖脂代谢；葡萄糖处置指数
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Short-term continuous subcutaneous insulin infusion combined with metformin and semaglutide in the treatment of type 2 diabetes mellitus

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Abstract: Objective　To observe the effect of short-term continuous subcutaneous insulin infusion (CSII) combined with metformin and semaglutide in the remission of type 2 diabetes mellitus (T2DM), glycolipid metabolism, islet β cell function, and weight. **Methods**　A total of 42 T2DM patients from the Department of Endocrinology at Geriatric Hospital of Nanjing Medical University were enrolled from September 2022 to December 2023. These patients were given 7-day CSII for intensive therapy during hospitalization, then combined with metformin and semaglutide, and were followed up for 48 weeks. The rate of diabetes remission was calculated. Changes of glycolipid metabolism indicators, islet β cell function, and body mass were compared between remission group and non-remission group. **Results**　After short-term treatment with CSII combined with metformin and semaglutide, the remission rate of T2DM was 54.76% at the 48th of follow-up. Compared with non-remission group, remission group showed more significant improvements in fasting blood glucose, glycated hemoglobin (HbA_{1C}), and glycated albumin at the 12th, 24th, and 36th weeks of follow-up ($P<0.05$), and the Disposal Index significantly increased at the 12th week ($P<0.05$). During the follow-up period, body mass and waist circumference decreased significantly ($P<0.05$), and high density lipoprotein cholesterol increased significantly ($P<0.05$). Univariate logistic regression analysis revealed that baseline 2-hour postprandial

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blood glucose (*OR*=1.204, 95% *CI*: 1.003-1.446) and medication duration (*OR*=0.386, 95% *CI*: 0.229-0.650) were influencing factors for remission of T2DM (*P*<0.05). **Conclusion** Short-term CSII combined with metformin and semaglutide can achieve higher rate of T2DM remission. Combination therapy can correct glycolipid metabolism dysfunction, improve islet β cell function and reduce body weight.

Keywords: Insulin intensive therapy; Type 2 diabetes mellitus; Diabetes remission; Metformin; Semaglutide; Continuous subcutaneous insulin infusion; Glycolipid metabolism; Glucose disposal rate

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有研究证实部分2型糖尿病(type 2 diabetes mellitus,T2DM)患者经干预后可逆转高血糖状态,实现糖尿病缓解[1]。持续皮下胰岛素输注(continuous subcutaneous insulin infusion,CSII)已被推荐作为糖尿病逆转治疗的首选方案[2]。SUSTAIN系列研究发现,经司美格鲁肽治疗后患者糖化血红蛋白(glycated hemoglobin,HbA_{1C})显著降低,部分患者实现血糖正常化[3],提示其具有诱导糖尿病缓解的潜力。本研究通过观察T2DM患者经短期CSII联合二甲双胍与司美格鲁肽治疗后糖尿病缓解、糖脂代谢及体质量的变化,旨在为糖尿病缓解治疗提供临床新策略。

1 对象与方法

1.1 *研究对象* 选取2022年9月至2023年12月于南京医科大学附属老年医院内分泌科住院的42例T2DM患者作为研究对象。纳入标准:(1)年龄>18岁;(2)HbA_{1C}≥7.5%;(3)糖尿病病程<5年;(4)未服用降糖药物或仅服用二甲双胍;(5)身体质量指数(body mass index,BMI)≥18.5 kg/m^2。排除标准:(1)1型糖尿病、成人晚发自身免疫性糖尿病或继发性糖尿病;(2)糖尿病急性并发症、严重慢性并发症;(3)影响HbA_{1C}水平的各类型贫血;(4)空腹C肽< 1.2 ng/mL;(5)严重心、肝、肾疾病;(6)严重感染性疾病未控制;(7)使用影响血糖的药物,如糖皮质激素、抗精神病药物等;(8)有认知功能障碍或不能配合研究及随访;(9)合并恶性肿瘤等疾病,预期寿命<5年。本研究经南京医科大学附属老年医院伦理委员会审核批准(伦理号:2022-019-3),所有研究对象均签署知情同意书。

1.2 *研究方法* 收集患者年龄、糖尿病病程、身高、体质量等一般资料,计算BMI。对纳入患者进行生活方式指导,包括个体化饮食及运动指导。入院后予7天胰岛素泵短期持续皮下输注强化治疗,排除禁忌后予盐酸二甲双胍片口服(中美上海施贵宝制药,国药准字H20023370,0.5g/次,2~3次/天)与司美格鲁肽注射液皮下注射[(丹麦诺和诺德,国药准字SJ20210014,规格:1.34 mg/mL,1.5 mL;国药准字SJ20210015,规格:1.34 mg/mL,3 mL),初始剂量为每周0.25 mg,4周后调整为每周0.5 mg,剂量最大可增加至每周1.0 mg联合治疗]。

出院后患者居家进行血糖监测,第2周行电话随访,询问方案依从性及药物不良反应等,胃肠道反应严重无法耐受者不纳入疗效分析。此后每月行电话随访,收集空腹血糖(fasting blood glucose,FBG)和餐后2小时血糖(2-hour postprandial blood glucose,2hPBG),并加强饮食及运动指导。出院后每12周至门诊复诊,行口服葡萄糖耐量试验(oral glucose tolerance test,OGTT)、血生化、血脂等检验,记录腰围、BMI、HbA_{1C}、总胆固醇、三酰甘油、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)、丙氨酸氨基转移酶、天冬氨酸氨基转移酶、谷氨酰转移酶,计算估算肾小球滤过率(estimated glomerular filtration rate,eGFR)和葡萄糖处置指数(disposition index,DI)。对于达到停药标准的患者予停药观察,嘱其坚持生活方式干预,12周后门诊评估是否达到缓解标准。当患者空腹血糖超过高血糖标准时需返院治疗,48周后结束随访。停药标准为FBG≤6.0 mmol/L且2hPBG≤8.0 mmol/L。糖尿病缓解诊断标准为停用降糖药物至少3个月后HbA_{1C}<6.5%,或FBG<7.0 mmol/L作为替代标准[4]。停药后达到缓解标准的患者为缓解组,随访48周内未停药或停药后未达到缓解标准的患者为未缓解组。比较两组间糖脂代谢、胰岛β细胞功能(DI)、腰围、BMI及体质量变化。

1.3 *统计学方法* 采用SPSS 27.0进行统计分析。正态分布计量资料以$\bar{x}\pm s$表示,组内比较采用t检验;多时间点比较采用重复测量方差分析,两两比较采用LSD-t检验。非正态分布的计量资料以$M(Q_1,Q_3)$表示,两组间比较采用秩和检验,重复测量资料采用Brunner非参数模型分析组间效应、时间效应及组间×时间交互效应,若某效应显著,采用Bonferroni校正的配对Wilcoxon符号秩检验进行两两比较。计数资

料以例(%)表示,组间比较采用 χ^2 检验,组内多时间点比较采用 Cochran Q 检验,两两比较采用 McNemar 检验,显著性水平采用 Bonferroni 法校正。采用单因素 logistic 回归分析确定糖尿病缓解的影响因素。以 P<0.05 为差异有统计学意义。

2　结　果

2.1　两组患者基线特征　根据随访结果,缓解组患者 23 例,未缓解组患者 19 例,缓解率为 54.76%。缓解组 2hPBG 及 BMI 显著高于未缓解组(P<0.05),其余基线资料比较差异无统计学意义(P>0.05)。见表 1。

2.2　两组糖代谢比较　两组 FBG、HbA_{1C}、糖化白蛋白存在显著时间效应(P<0.05),FBG 存在显著交互效应(P<0.05)。随访期间两组糖代谢指标均较基线显著改善(P<0.05)。缓解组治疗 12 周、24 周、36 周糖代谢指标均较同时间点未缓解组显著改善(P<0.05)。见表 2。

2.3　两组体质量与腰围比较　两组体质量差值、腰围差值存在显著组间、交互效应(P<0.05),随访期间缓解组体质量、腰围较未缓解组下降更为显著(P<0.05)。两组 BMI 差值存在显著时间效应(P<0.05),缓解组随访 12 周、48 周 BMI 较未缓解组下降更为显著(P<0.05)。见表 3。

2.4　两组血脂指标比较　两组总胆固醇差值存在显著时间效应(P<0.05),缓解组随访 12 周、36 周总胆固醇较未缓解组下降更为显著(P<0.05)。两组 HDL-C 差值存在显著组间、时间、交互效应(P<0.05),随访期间缓解组 HDL-C 差值较未缓解组显著升高(P<0.05)。见表 4。

2.5　两组胰岛β细胞功能比较　两组 DI 存在显著时间、交互效应(P<0.05)。随访期间两组 DI 均较基线显著升高(P<0.05),其中缓解组治疗 12 周 DI 较同时间点未缓解组显著升高(P<0.05)。见表 5。

2.6　T2DM 缓解影响因素　将上述缓解组和未缓解基线比较差异有统计学意义的指标(BMI、2hPBG)以及用药时长进一步纳入单因素 logistic 回归分析发现用药时长(OR=0.386, 95%CI: 0.229~0.650)及基线 2hPBG(OR=1.204, 95%CI: 1.003~1.446)是 T2DM 缓解的影响因素(P<0.05)。

表 1　缓解组与未缓解组基线特征

Tab.1　Baseline characteristics between remission group and non-remission group

临床特征	缓解组(n=23)	未缓解组(n=19)	$t/\chi^2/Z$ 值	P 值
年龄(岁)[a]	52.52±12.00	57.00±12.44	1.401	0.244
性别(男/女,例)	12/11	9/10	0.096	0.757
病程(月)[b]	3.00(0.33,24.00)	3.00(1.00,36.00)	0.482	0.630
二甲双胍使用史[例(%)]	8(34.78)	8(42.11)	0.237	0.627
体质量(kg)[b]	77.00(66.00,84.00)	70.00(64.00,75.00)	1.555	0.120
腰围(cm)[a]	94.13±10.72	90.05±8.82	1.762	0.192
BMI (kg/m^2)[b]	26.80(24.39,29.41)	24.70(22.68,26.03)	2.009	0.045
收缩压(mmHg)[a]	136.39±15.31	134.26±14.70	0.208	0.651
舒张压(mmHg)[a]	82.61±9.40	80.32±11.52	0.505	0.481
入院时 FBG(mmol/L)[a]	9.05±3.18	8.58±3.58	0.200	0.657
2hPBG(mmol/L)[a]	14.93±4.57	12.29±2.97	4.711	0.036
HbA_{1C}(%)[a]	9.74±1.99	9.46±1.91	0.214	0.646
糖化白蛋白(%)[a]	23.39±10.07	21.76±5.50	0.399	0.531
总胆固醇(mmol/L)[a]	4.64±1.39	5.00±1.25	0.789	0.380
三酰甘油(mmol/L)[a]	1.88±1.13	1.56±0.63	1.206	0.279
HDL-C(mmol/L)[a]	2.79±0.99	3.00±0.88	0.531	0.470
HDL-C(mmol/L)[a]	1.01±0.28	1.09±0.19	1.044	0.313
丙氨酸氨基转移酶(u/L)[b]	32.00(17.00,47.00)	21.00(14.00,42.00)	0.657	0.511
天冬氨酸氨基转移酶(u/L)[b]	21.00(14.00,32.00)	19.00(14.00,28.00)	0.569	0.569
谷氨酰转移酶(u/L)[b]	35.00(25.00,48.00)	26.00(19.00,50.00)	0.582	0.561
血尿酸(μmol/L)[b]	337.00(258.00,378.00)	286.00(269.00,339.00)	1.036	0.300
血肌酐(μmol/L)[a]	64.13±15.65	57.36±20.11	1.507	0.227
eGFR[mL/(min·1.73 m^2)][a]	104.20±16.47	103.09±17.84	0.044	0.834

注:[a]数据以 $\bar{x}\pm s$ 表示;[b]数据以 $M(Q_1,Q_3)$ 表示。

表2　缓解组与未缓解组糖代谢指标比较　($\bar{x}\pm s$)

Tab.2　Comparison of glucose metabolism indicators between remission group and non-remission group　($\bar{x}\pm s$)

时间点	FBG(mmol/L)		HbA_{1C}(%)		糖化白蛋白(%)	
	缓解组(n=23)	未缓解组(n=19)	缓解组(n=23)	未缓解组(n=19)	缓解组(n=23)	未缓解组(n=19)
基线	8.47±2.88	7.64±1.56	9.74±1.99	9.46±1.91	23.39±10.07	21.76±5.50
12周	5.57±0.53^{ab}	6.46±0.91^{a}	5.88±0.46^{ab}	6.41±0.40^{a}	12.19±1.98^{ab}	14.18±3.72^{a}
24周	5.65±0.58^{ab}	6.22±0.78^{a}	5.70±0.43^{ab}	6.26±0.40^{a}	12.87±1.71^{ab}	14.32±1.78^{a}
36周	5.88±0.82^{ab}	6.39±0.77^{a}	5.93±0.41^{ab}	6.41±0.46^{a}	13.17±1.38^{ab}	14.42±1.99^{a}
48周	6.22±1.06^{a}	6.67±0.87^{a}	6.23±0.70^{a}	6.60±0.60^{a}	13.49±2.04^{a}	14.53±1.39^{a}
$F_{组间}/F_{时间}/F_{交互}$	1.937/23.225/4.869		4.302/84.256/3.789		0.369/72.015/2.655	
$P_{组间}/P_{时间}/P_{交互}$	0.181/<0.001/0.041		0.053/<0.001/0.067		0.551/<0.001/0.120	

注：与同组基线比较，^{a}P<0.05；与同时间点未缓解组比较，^{b}P<0.05。

表3　缓解组与未缓解组体质量和腰围比较　[$M(Q_1,Q_3)$]

Tab.3　Comparison of weight and waist circumference between remission group and non-remission group　[$M(Q_1,Q_3)$]

时间点	体质量差值(kg)		腰围差值(cm)		BMI差值(kg/m^2)	
	缓解组(n=23)	未缓解组(n=19)	缓解组(n=23)	未缓解组(n=19)	缓解组(n=23)	未缓解组(n=19)
12周	−4.00(−7.00,−2.90)^{a}	−3.30(−5.00,2.00)	−6.00(−9.00,−3.00)^{a}	−1.00(−2.00,0)	−1.70(−2.44,−1.10)^{a}	−0.95(−1.65,0.96)
24周	−4.80(−7.30,−3.00)^{a}	−4.00(−7.50,0.10)	−7.00(−11.00,−3.00)^{a}	−2.00(−5.00,3.00)	−1.80(−2.74,−1.31)	−1.27(−2.40,−0.14)
36周	−4.10(−7.00,−2.40)^{a}	−4.20(−5.40,0.30)	−3.00(−8.00,−2.00)^{a}	−3.00(−9.00,−1.00)	−1.70(−2.30,−0.87)	−1.42(−1.83,0.06)
48周	−4.80(−7.10,−2.00)^{a}	−0.10(−4.10,0.30)	−7.50(−10.00,0)^{a}	−2.00(−6.00,12.00)	−1.63(−2.40,−0.18)^{a}	−0.42(−1.50,0.28)
$W_{组间}/W_{时间}/W_{交互}$	17.856/2.235/6.920		4.998/1.818/9.987		2.476/4.757/3.156	
$P_{组间}/P_{时间}/P_{交互}$	<0.001/0.525/0.008		0.025/0.177/0.016		0.116/0.029/0.076	

注：与同时间点未缓解组比较，^{a}P<0.05。

表4　缓解组与未缓解组血脂指标比较　[$M(Q_1,Q_3)$]

Tab.4　Comparison of lipid indicators between remission group and non-remission group　[$M(Q_1,Q_3)$]

时间点	总胆固醇差值(mmol/L)		HDL-C差值(mmol/L)	
	缓解组(n=23)	未缓解组(n=19)	缓解组(n=23)	未缓解组(n=19)
12周	−0.80(−1.94,0.11)^{a}	−0.79(−2.23,0)	0.11(−0.08,0.29)^{a}	0.02(−0.16,0.20)
24周	−0.06(−1.63,0.22)	−0.55(−1.83,−0.13)	0.22(−0.02,0.35)^{a}	0.17(−0.07,0.23)
36周	−0.47(−1.22,0.72)^{a}	−0.58(−1.57,0.43)	0.32(0.08,0.54)^{a}	0.01(−0.07,0.28)
48周	−0.40(−1.22,2.14)	−0.28(−1.38,0.45)	0.25(0.00,0.68)^{a}	0.02(−0.11,0.27)
$W_{组间}/W_{时间}/W_{交互}$	0.002/18.457/2.171		4.272/24.363/7.067	
$P_{组间}/P_{时间}/P_{交互}$	0.964/<0.001/0.141		0.039/<0.001/0.008	

注：与同时间点未缓解组比较，^{a}P<0.05。

表5　缓解组与未缓解组DI比较　[$M(Q_1,Q_3)$]

Tab.5　Comparison of DI between remission group and non-remission group　[$M(Q_1,Q_3)$]

时间点	缓解组(n=23)	未缓解组(n=19)
基线	0.18(0.01,0.36)	0.28(0.15,0.66)
12周	0.57(0.42,0.86)^{ab}	0.39(0.21,0.51)^{a}
24周	0.78(0.43,1.08)^{a}	0.44(0.29,0.74)^{a}
36周	0.52(0.42,0.88)^{a}	0.47(0.31,0.73)^{a}
48周	0.50(0.35,0.91)^{a}	0.39(0.26,0.65)^{a}
$W_{组间}/W_{时间}/W_{交互}$	2.577/23.863/9.327	
$P_{组间}/P_{时间}/P_{交互}$	0.108/<0.001/0.002	

注：与同组基线比较，^{a}P<0.05；与同时间点未缓解组比较，^{b}P<0.05。

3　讨　论

据国际糖尿病联盟报告，我国是全球糖尿病患病人数最多的国家[5]，2024年我国成人糖尿病患病率为11.9%[6]，预计2050年我国糖尿病患病人数仍居世界首位。我国糖尿病防控形势严峻，早期筛查、及时干预，控制血糖达标甚至早期实现缓解尤为重要。

二甲双胍是T2DM一线首选治疗用药，也是联合治疗的基础用药。胰岛素强化治疗是强化血糖控制的重要手段，其核心机制是通过补充外源胰岛素，迅速纠正高糖状态，减轻高糖毒性，降低体内炎症因子水平[7]，改善机体慢性炎症，可显著降低大血管事件和心肌梗死的发生风险，进而改善患者预后[8]。同时，胰岛素强化治疗能够保护并促进胰岛β细胞功能恢复，显著提高β细胞的胰岛素分泌能力，改善靶器官对胰岛素的敏感性[9]。经过2~3周的胰岛素强化治疗后，患者胰岛素第一时相的分泌异常得到纠正[10]，在治疗结束后的较长时间内，血糖仍能保持在令人满意

的水平。司美格鲁肽以葡萄糖浓度依赖的方式促进胰岛β细胞分泌胰岛素，同时抑制胰高血糖素分泌，能够有效改善患者空腹及餐后血糖，显著降低HbA_{1c}，并降低血糖波动，降低低血糖事件的发生风险，从而实现对血糖的长期稳定调控[3]。此外，司美格鲁肽还通过抑制下丘脑摄食中枢，降低患者食欲，增加饱腹感，延缓胃排空，减少食物吸收，促进体质量减轻[11]。相关研究证实司美格鲁肽通过改善脂质代谢，降低与动脉粥样硬化相关的蛋白水平，可显著降低T2DM患者发生主要心血管不良事件的风险[12]。

已有研究证实，经4周利拉鲁肽联合甘精胰岛素、12周甘精胰岛素联合利司那肽与二甲双胍治疗后，第48周时T2DM缓解率分别为42.74%、22.8%[9,13]，而本研究中第48周时T2DM缓解率达54.76%。分析原因可能是本研究联合方案中药物作用机制的协同效应：短期胰岛素强化治疗能够纠正高糖状态，解除高糖毒性对胰岛β细胞的抑制进而恢复其受损的分泌功能[9]，同时二甲双胍通过延缓葡萄糖吸收、抑制肝糖原输出并提高外周组织对胰岛素的敏感性以增强降糖效果[14]，而司美格鲁肽则通过促进胰岛β细胞分泌、抑制胰高血糖素释放以增强血糖调控[15]，并进一步通过显著减重作用改善胰岛素抵抗[11]，从而提高靶器官对胰岛素的敏感性，上述机制共同作用形成协同治疗效应。

《缓解2型糖尿病中国专家共识》[16]提出“ABCD”原则以预测糖尿病缓解可能性，其中“A”为胰岛素自身抗体、“B”为BMI、“C”为C肽、“D”为病程，其它研究也发现基线HbA_{1c}与T2DM缓解存在相关性[17]。本研究中缓解组基线BMI较未缓解组高，符合预测原则，但病程及基线HbA_{1c}差异无统计学意义。本研究经单因素logistic回归分析发现基线2hPBG及用药时长是T2DM缓解的影响因素，血糖明显升高可引起胰岛β细胞分泌功能受损。本研究中，缓解组基线2hPBG显著高于未缓解组，基线DI低于未缓解组，提示缓解组患者基线时胰岛β细胞功能受损更为严重。然而缓解组DI较基线显著升高，β细胞功能显著改善，这可能是因为缓解组胰岛β细胞暴露于高糖环境时间相对较短，胰岛β细胞尚未形成不可逆损害，因此经联合方案治疗后，受损β细胞的分泌功能得到及时修复，从而提高缓解可能性。本研究中，用药时长也是影响T2DM缓解的重要因素，在随访的各时期，两组患者DI均较基线升高，说明用药时间的延长可对胰岛β细胞功能产生持续改善作用，可巩固联合方案的治疗效应，从而提高T2DM的缓解率。然而进一步行多因素回归分析则差异无统计学意义，校正混杂因素后结果差异仍无统计学意义。这可能是因为本研究仅纳入42例患者，样本量有限导致多因素模型检验效能不足，最终采用单因素回归分析结果，后续需在大样本人群中验证基线2hPBG及用药时长与T2DM缓解相关性。

糖尿病患者发生动脉粥样硬化心血管疾病的风险显著高于非糖尿病人群[18]，低HDL-C水平是动脉粥样硬化心血管疾病的独立危险因素，而较高的LDL-C水平与全因死亡率和心血管疾病死亡率增加有关[19]。本研究中经联合方案治疗后患者HDL-C较基线升高，说明该联合方案对糖尿病患者血脂管理具有一定疗效。

本研究中两组间各指标显著差异性主要出现在第12、24周，这可能是因为联合方案对血糖及体质量改善的持续作用以及缓解组中患者非同步停药。与未缓解组相比，同一时期缓解组中部分患者可能已停药超12周，这部分患者各项指标可能随停药时间的延长较用药期间回升，导致两组间部分指标差异无统计学意义。

综上所述，短期持续皮下胰岛素输注联合二甲双胍与司美格鲁肽可显著降糖减重调脂，并实现更高比例的糖尿病缓解。本研究也存在以下不足：（1）本研究是一项小样本自身前后对照的单臂研究，后续需在更大规模的随机对照研究中进一步验证结果。（2）由于时间限制，未能进一步观察长期缓解和复发情况，后续可延长随访时间以观察联合方案的长期疗效。

利益冲突　无

参考文献

[1] Liu YJ, Chen Y, Ma JH, et al. Dapagliflozin plus calorie restriction for remission of type 2 diabetes: multicentre, double blind, randomised, placebo controlled trial [J]. BMJ, 2025, 388: e081820.

[2] 中国胰岛素分泌研究组. 短期胰岛素强化治疗逆转2型糖尿病专家共识[J]. 中华糖尿病杂志, 2021, 13(10): 949-959.

[3] Kellerer M, Kaltoft MS, Lawson J, et al. Effect of once-weekly semaglutide versus thrice-daily insulin aspart, both as add-on to metformin and optimized insulin glargine treatment in participants with type 2 diabetes (SUSTAIN 11): a randomized, open-label, multinational, phase 3b trial [J]. Diabetes Obes Metab, 24(9): 1788-1799.

[4] Riddle MC, Cefalu WT, Evans PH, et al. Consensus report: definition and interpretation of remission in type 2 diabetes [J]. J Clin Endocrinol Metab, 2022, 107(1): 1-9.

[5] 宋小刚, 陈子仪, 马霞, 等. 脂毒性在糖尿病心肌病发病中作用的研究进展[J]. 中国病理生理杂志, 2022, 38(11): 2106-2112.

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研究, 2025, 38(4): 507-510.
[12] Hu MM, Shu HB. Mitochondrial DNA-triggered innate immune response: mechanisms and diseases[J]. Cell Mol Immunol, 2023, 20(12): 1403-1412.
[13] 陈待庆, 郑健生, 谢可, 等. 系统免疫炎症指数、C反应蛋白/清蛋白比值评估糖尿病足溃疡病情严重程度和预后的价值[J]. 中国感染控制杂志, 2023, 22(8): 901-906.
[14] Zhang HH, Yan Z, Zhu JY, et al. Extracellular mitochondrial-derived vesicles affect the progression of diabetic foot ulcer by regulating oxidative stress and mitochondrial dysfunction[J]. Adv Sci, 2025, 12(10): 2407574.
[15] Riley JS, Tait SW. Mitochondrial DNA in inflammation and immunity[J]. EMBO Rep, 2020, 21(4): e49799.
[16] de Oliveira Matos A, dos Santos Dantas PH, Silva-Sales M, et al. TREM-1 isoforms in bacterial infections: to immune modulation and beyond[J]. Crit Rev Microbiol, 2021, 47(3): 290-306.
[17] Metthew Lam LK, Murphy S, Kokkinaki D, et al. DNA binding to TLR9 expressed by red blood cells promotes innate immune activation and Anemia[J]. Sci Transl Med, 2021, 13(616): eabj1008.
[18] Niu ZX, Bao L, Chen J. Upregulation of TLR9 may contribute to activation of microglia and painful diabetic neuropathy *via* the p38 MAPK pathway in rats[J]. Histol Histopathol, 2022, 37(1): 81-91.
[19] Siskind S, Brenner M, Wang P. TREM-1 modulation strategies for sepsis[J]. Front Immunol, 2022, 13: 907387.
[20] Nguyen TTT, Yoon HK, Kim YT, et al. Tryptophanyl-tRNA synthetase 1 signals activate TREM-1 *via* TLR2 and TLR4[J]. Biomolecules, 2020, 10(9): 1283.
[21] Qin Q, Liang LJ, Xia YQ. Diagnostic and prognostic predictive values of circulating sTREM-1 in sepsis: a meta-analysis[J]. Infect Genet Evol, 2021, 96: 105074.
[22] Liu H, Fan HL, He PC, et al. Prohibitin 1 regulates mtDNA release and downstream inflammatory responses[J]. EMBO J, 2022, 41(24): EMBJ2022111173.
[23] Ma XM, Geng K, Law BY, et al. Lipotoxicity-induced mtDNA release promotes diabetic cardiomyopathy by activating the cGAS-STING pathway in obesity-related diabetes[J]. Cell Biol Toxicol, 2023, 39(1): 277-299.
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(上接第845页)

[6] 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.
[7] Esser N, Utzschneider KM, Kahn SE. Early beta cell dysfunction *vs* insulin hypersecretion as the primary event in the pathogenesis of dysglycaemia[J]. Diabetologia, 2020, 63(10): 2007-2021.
[8] Luo SH, Zheng XY, Bao W, et al. Real-world effectiveness of early insulin therapy on the incidence of cardiovascular events in newly diagnosed type 2 diabetes[J]. Sig Transduct Target Ther, 2024, 9: 154.
[9] McInnes N, Hall S, Hramiak I, et al. Remission of type 2 diabetes following a short-term intensive intervention with insulin glargine, sitagliptin, and metformin: results of an open-label randomized parallel-design trial[J]. Diabetes Care, 2022, 45(1): 178-185.
[10] Liu LH, Ke WJ, Li H, et al. Intense simplified strategy for newly diagnosed type 2 diabetes in patients with severe hyperglycaemia: multicentre, open label, randomised trial[J]. BMJ, 2024, 387: e080122.
[11] 王绍欣, 韩丽萍. 司美格鲁肽减重作用研究进展[J]. 中华糖尿病杂志, 2024, 16(S2): 266-269.
[12] Nauck MA, Quast DR. Cardiovascular safety and benefits of semaglutide in patients with type 2 diabetes: findings from SUSTAIN 6 and PIONEER 6[J]. Front Endocrinol, 2021, 12: 645566.
[13] 卓雅芬, 孙志纯, 洪真真, 等. 利拉鲁肽联合甘精胰岛素治疗对新诊断2型糖尿病患者长期临床缓解的疗效观察[J]. 中国糖尿病杂志, 2021, 29(10): 733-737.
[14] Rena G, Hardie DG, Pearson ER. The mechanisms of action of metformin[J]. Diabetologia, 2017, 60(9): 1577-1585.
[15] Papakonstantinou I, Tsioufis K, Katsi V. Spotlight on the mechanism of action of semaglutide[J]. Curr Issues Mol Biol, 2024, 46(12): 14514-14541.
[16] 《缓解型糖尿病中国专家共识》编写专家委员会. 缓解2型糖尿病中国专家共识[J]. 中国全科医学, 2021, 24(32): 4037-4048.
[17] Holman N, Wild SH, Khunti K, et al. Incidence and characteristics of remission of type 2 diabetes in England: a cohort study using the national diabetes audit[J]. Diabetes Care, 2022, 45(5): 1151-1161.
[18] Xiao Y, Yu BL, Chao C, et al. Chinese expert consensus on blood lipid management in patients with diabetes (2024 edition)[J]. J Transl Intern Med, 2024, 12(4): 325-343.
[19] 中国血脂管理指南修订联合专家委员会. 中国血脂管理指南(基层版2024年)[J]. 中国全科医学, 2024, 27(20): 2429-2436.
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