Noninferiority Effects on Glycemic Control and β -Cell Function Improvement in Newly Diagnosed Type 2 Diabetes Patients: Basal Insulin Monotherapy Versus Continuous Subcutaneous Insulin Infusion Treatment

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Abstract

Aims: In newly diagnosed type 2 diabetes mellitus (T2DM) patients, short-term insulin therapy might improve β -cell function and glycemic control. This study aimed to compare the effects of basal insulin monotherapy with continuous subcutaneous insulin infusion (CSII) treatment.

Methods: Fifty-nine cases of newly diagnosed T2DM patients with fasting plasma glucose of 9.0–16.7 mmol/L were recruited into this study. They were hospitalized and randomly assigned to a basal insulin monotherapy group ($n=27$) or a CSII group ($n=32$). Insulin dosage was titrated according to fasting capillary blood glucose levels, and treatment was stopped after 2 weeks. Intravenous glucose tolerance tests were performed, and blood glucose, insulin, C-peptide, and lipid profiles were measured before therapy and 2 days after therapy withdrawal.

Results: Both treatments reduced fasting and postprandial blood glucose levels (after treatment vs. baseline, both $P<0.05$). Fasting glycemic control target was achieved in 52 cases (88.14%) with 2 weeks of insulin treatment, and there were no significant differences between the glargine and CSII groups ($P=0.059$). The time to achieve fasting glycemic target in the CSII group was shorter than that in the glargine group ($P<0.01$). Plasma lipid profiles such as triglycerides and total cholesterol also decreased significantly after the intervention. Overall β -cell function improved significantly after insulin intervention ($P<0.01$). Variation did not differ between two groups, nor did the effects on insulin and C-peptide secretion ($P>0.05$).

Conclusions: The effect of basal insulin monotherapy was similar to that of CSII, and thus basal insulin monotherapy might be a reasonable alternative to CSII for initial insulin therapy in newly diagnosed T2DM patients.

Introduction

INSULIN RESISTANCE AND progressive β -cell deterioration are the two main pathophysiological mechanisms of type 2 diabetes mellitus (T2DM).^{1,2} The UK Prospective Diabetes Study has shown that β -cell function begins to deteriorate before type 2 diabetes is diagnosed and often occurs years before patients demonstrate clinical symptoms.^{3,4} In most T2DM patients, metabolic control and β -cell function progressively deteriorate as the duration of diabetes increases, and this deterioration can be explained by decreased insulin secretion by β -cells.^{1,2,4} As β -cell function declines, most patients will ultimately need insulin therapy, and insulin treatment could be of benefit as it provides relative “ β -cell

rest.” At present, insulin is the most important drug available to achieve tight glycemic control; however, when and how to initiate insulin treatment in T2DM still remain controversial.

Because the loss of acute insulin response (AIR) is a quite common defect in the pathogenesis of newly diagnosed T2DM, it may require specific therapeutic intervention.³ Several clinical trials in different ethnic population have suggested that early insulin treatment could preserve endogenous insulin secretion and improve metabolic control.^{5–9} Our previous study has also shown that short-term intensive insulin therapy can induce long-term glycemic control in newly diagnosed T2DM patients with severe hyperglycemia. The improvement of β -cell function, especially the restoration

of first-phase insulin secretion, could be responsible for the remission.^{10,11}

However, insulin is often withheld from people with T2DM until they are unresponsive to a combination of lifestyle changes and one or more oral antidiabetes drugs (OADs). This is partly due to physicians' and patients' psychological resistance to initiation of insulin,¹² the risk of hypoglycemia, and concern about insulin injection or restrictions of lifestyle. With T2DM becoming a major chronic disease and a global health disaster, it forces us to come up with an ideal strategy to cope with it. The latest national survey in China showed the prevalence of total diabetes was 9.7%, which amounts to nearly 92.4 million Chinese adults suffering from diabetes.¹³ Although clinical guidelines recommend target glycosylated hemoglobin (HbA_{1c}) values of <7% (European Association for the Study of Diabetes criterion) for persons with diabetes, unfortunately less than one-third of patients globally can achieve this target.^{14,15} Failure to reach glycemic target may be partly explained by two reasons: one is the progressive deterioration in the natural course of β -cell function,^{1,2} and the other is a delay in initiating insulin therapy.¹⁵

Moreover, in the previous studies, continuous subcutaneous insulin infusion (CSII) or multiple daily insulin injections were used as initial insulin treatment protocols, which are expensive and complex and could not be widely adopted in clinical practice, especially for outpatients. Therefore, we performed this randomized, open-label, parallel-group trial of two short-term insulin therapy programs with basal insulin monotherapy or CSII treatment. The aim of this observational study was to compare the effects of two insulin therapy programs on glycemic control and β -cell function in patients with newly diagnosed T2DM.

Subjects and Methods

Patients

Fifty-nine patients (30 men and 29 women) at The Third Affiliated Hospital of Sun Yat-sen University (Guangzhou, Guangdong, China) hospitalized with newly diagnosed T2DM (fasting plasma glucose [FPG], 9.0–16.7 mmol/L) from November 2007 to December 2008 were recruited into the study. Diabetes mellitus was diagnosed according to the criteria published by the World Health Organization in 1999. The patients had no history of using any antihyperglycemic drugs and were negative for anti-glutamic acid decarboxylase antibodies. Patients were excluded from the trial if they were unlikely to adhere to the protocol and if they had acute or severe chronic diabetes complications or severe intercurrent illness or were pregnant. This work was approved by the ethical committees of the Third Affiliated Hospital of Sun Yat-sen University, and all subjects gave informed consent.

Study design and treatment

After 2 weeks of diet control and run-in, patients were hospitalized and assigned to a basal insulin monotherapy group ($n = 27$) or a CSII group ($n = 32$) according to the random number method. Patients in the basal insulin monotherapy group received insulin glargine (Lantus®, Sanofi-Aventis, Paris, France) injection once daily at bedtime. Patients in the CSII group received rapid-acting insulin analog (insulin Aspart®, Novo Nordisk, Bagsværd, Denmark) as basal and

prandial insulin with an insulin pump (Paradigm® 712, Medtronic, Minneapolis, MN). Total initial insulin doses were 0.3 IU/kg for the basal insulin group and 0.5 IU/kg in the CSII group (including basal and boluses insulin, as usual). The doses were titrated every day in order to achieve the fasting glycemic target, which was defined as fasting capillary blood glucose varying between 4.4 mmol/L and 6.1 mmol/L, regardless of the patients' postprandial blood glucose levels. During the intervention, their capillary blood glucose was monitored by nurses using a blood glucometer (OneTouch® Ultra®, LifeScan, Milpitas, CA) at least seven times per day, including fasting, before lunch/dinner, 2 h postprandial (after breakfast, lunch, and supper), and at bedtime. A continuous glucose monitoring system (CGMS® Gold™, Medtronic) was used in 18 cases (eight cases in the basal insulin group and 10 cases in the CSII group). Intervention was stopped after 2 weeks. After interventions were stopped, patients were instructed to continue diet and physical exercise or received OAD treatment according to their plasma glucose levels. Hypoglycemia was defined as capillary blood glucose ≤ 3.9 mmol/L with or without clinical symptoms. The primary end point was the time when fasting capillary blood glucose reached the target; the second end point was the effect of different insulin interventions on β -cell function and glycemic control in these patients.

Assessments

Before and after treatment, fasting blood samples were obtained after an overnight fasting for measurement of glucose, HbA_{1c}, and lipid levels. Before intervention and 2 days after insulin cessation, all patients received an intravenous glucose tolerance test (IVGTT) using 25 g of glucose (50 mL of 50% glucose), and serum samples were obtained prior to and 1, 2, 4, 6, and 10 min after the intravenous glucose load to measure insulin and C-peptide concentrations.

Routine clinical biochemical analyses were performed in the hospital laboratory. FPG was measured by the glucose oxidase method. Plasma triglycerides, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol were measured by the oxides method with an automatic biochemistry instrument. HbA_{1c} was assayed using the Bio-Rad (Hercules, CA) Variant HbA_{1c} assay. Plasma insulin and C-peptide levels were measured using a chemiluminescence enzyme-linked immunosorbent assay kit (Bioekon Inc., Beijing, China). The first-phase β -cell insulin secretion, which was calculated as the incremental trapezoidal area under the curve (AUC) for insulin and C-peptide during the first 10 min of the IVGTT, was used to assess the AIR. β -Cell function and insulin resistance were assessed by homeostasis model (HOMA-B and HOMA-IR, respectively) according to the following equations: $\text{HOMA-B} = (20 \times \text{fasting insulin}) / (\text{FPG} - 3.5)$ and $\text{HOMA-IR} = (\text{FPG} \times \text{fasting insulin}) / 22.5$.

Statistical analyses

Normally distributed and quantitative data were expressed as mean $\pm$ SD values. The experimental variables (triglycerides, very-low-density lipoprotein-cholesterol, insulin, and C-peptide) that were not normally distributed were expressed as median $\pm$ interquartile range values and log-transformed to improve data normality. Quantitative variable differences

between the two groups were compared by Student's *t* tests; the differences before and after treatment were analyzed with sample-paired Student's *t* test. The χ^2 test was performed to compare for discrete variables. All statistical analyses were conducted by using the SPSS version 13.0 statistical package (SPSS, Inc., Chicago, IL). A value of $P < 0.05$ was considered statistically significant.

Results

Patients studied

A total of 59 patients completed this research. None dropped out, and no serious adverse effects were observed during the intervention. Demographic and metabolic baseline characteristics of the two groups are summarized in Table 1. The two groups were well balanced, with HbA_{1c} averaging 10.85% and FPG averaging 12.9 mmol/L. There were no significant differences in age, sex, or plasma lipid profiles between the two groups.

Glycemic control and plasma lipid improvement

Table 2 depicts the variations in glycemic and plasma lipid profiles after two different insulin treatments. Among these patients, 52 cases achieved the glycemic control target, and there was no statistical difference between the two groups (88.89% in the basal insulin monotherapy group and 87.50% in the CSII group, $P = 0.059$). The time to achieve glycemic

target in the CSII group was shorter than that in the basal insulin group (3.8 ± 1.9 days vs. 5.4 ± 1.4 days), and the difference was statistically significant ($P < 0.01$). The lower rate of fasting glucose levels was similar between the two groups (7.61 ± 3.72 vs. 6.37 ± 3.93 mmol/L, $P > 0.05$). There was a great decrease in 2-h postprandial capillary blood glucose in both groups (before vs. after treatment, $P < 0.001$), but slightly more in the CSII group (11.1 ± 3.7 mmol/L vs. 9.1 ± 3.4 mmol/L, $P = 0.049$). Figure 1 depicts dynamic changes in fasting and daily average 2-h postprandial capillary blood glucose. From Figure 1 we can see that 2 weeks of insulin therapy could significantly decrease fasting and postprandial blood glucose. In addition, there was no difference in fasting capillary glucose levels after insulin treatment (5.66 ± 1.09 vs. 5.89 ± 1.22 mmol/L, $P > 0.05$), but patients in the CSII group had lower postprandial blood glucose levels (6.2 ± 0.9 vs. 10.2 ± 2.7 mmol/L, $P < 0.001$). HbA_{1c} decreased nearly 1% in 2 weeks, and there was no significant difference between the two groups.

Plasma lipid profiles and triglyceride and total cholesterol levels were decreased greatly after insulin treatment ($P < 0.01$) in both groups, and there was no significant difference between the two groups. Plasma low-density lipoprotein-cholesterol levels were significantly lowered in the CSII group (3.55 ± 0.93 vs. 3.09 ± 0.78 mmol/L, $P < 0.05$), whereas in the glargine group they were lowered, but without statistical difference (3.57 ± 0.94 vs. 3.42 ± 0.68 mmol/L, $P > 0.05$). Plasma high-density lipoprotein-cholesterol levels increased somewhat, but no significant difference was found before and after insulin treatment.

Effects on β -cell function

Figure 2 depicts the variations of plasma insulin and C-peptide changes during IVGTT before and after insulin treatment. Both were elevated after insulin treatment ($P < 0.05$), but there was no statistical difference between the two groups ($P > 0.05$). From Figure 3 we can see that the AIR, represented by AUC for insulin and AUC for C-peptide, was low in all patients before treatment (Fig. 3C). After 2 weeks of insulin therapy, AIR increased significantly ($P < 0.001$) (Fig. 3), indicating that β -cell function was partially recovered in most patients. HOMA-B improved greatly after insulin therapy, and HOMA-IR declined significantly in both groups ($P < 0.001$) (Table 2). No differences were found between the two groups before and after insulin treatment.

Insulin dosing

The daily dose of insulin was recorded every day. The maximum dose and final daily dose of insulin mean, respectively, the maximum dosing of insulin during the intervention and the final dose of insulin before the intervention stopped. These data are shown in Table 3. From these data, we can see both the maximum and final daily insulin doses were less in the basal insulin monotherapy group than in the CSII group.

Adverse side effects

During the insulin treatment period, no serious adverse side effects were observed in either group. There were no changes in liver and renal function before and after treatment.

TABLE 1. DEMOGRAPHIC AND METABOLIC BASELINE CHARACTERISTICS OF THE TWO PATIENT GROUPS

Variable	Basal insulin group	CSII group	Total
Male/female (n)	12/15	18/14	30/29
Age (years)	52.72 ± 8.54	48.90 ± 10.67	50.37 ± 9.82
BMI (kg/m^2)	25.11 ± 2.54	25.73 ± 3.91	25.46 ± 3.12
FPG (mmol/L)	13.27 ± 3.80	12.47 ± 3.7	12.88 ± 3.76
HbA _{1c} (%)	10.78 ± 2.57	10.93 ± 2.23	10.85 ± 2.40
Triglycerides (mmol/L) ^a	3.07 ± 1.78	2.92 ± 1.16	3.04 ± 1.21
Total cholesterol (mmol/L)	5.89 ± 1.03	5.65 ± 1.08	5.76 ± 0.94
LDL-C (mmol/L)	3.57 ± 0.94	3.55 ± 0.93	3.56 ± 0.94
HDL-C (mmol/L)	1.09 ± 0.26	1.15 ± 0.62	1.12 ± 0.45
AIR ($\mu\text{IU}/\text{mL}/\text{min}$) ^a	0.13 ± 2.96	-1.09 ± 4.46	-0.76 ± 2.52
AUC _{Ins} ($\mu\text{IU}/\text{mL}/\text{min}$) ^a	104.75 ± 44.98	114.89 ± 54.42	108.69 ± 50.27
AUC _{Cpep} (pmol/ mL/min) ^a	6.22 ± 1.65	6.96 ± 2.72	6.67 ± 2.13
HOMA-B ^a	26.7 ± 19.0	30.4 ± 18.7	28.72 ± 18.86
HOMA-IR ^a	6.02 ± 2.37	6.68 ± 2.97	6.38 ± 2.65

Data are mean $\pm$ SD unless otherwise indicated.

^aData are median $\pm$ IQR values. $P > 0.05$ compared with two groups.

AIR, acute insulin response; AUC_{Ins} and AUC_{Cpep}, area under the curve for insulin and C-peptide, respectively; BMI, body mass index; CSII, continuous subcutaneous insulin infusion; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HOMA-B and HOMA-IR, β -cell function and insulin resistance, respectively, which were assessed by homeostasis model according to the equations $\text{HOMA-B} = (20 \times \text{fasting insulin}) / (\text{FPG} - 3.5)$ and $\text{HOMA-IR} = (\text{FPG} \times \text{fasting insulin}) / 22.5$; LDL-C, low-density lipoprotein cholesterol.

TABLE 2. DATA AFTER TREATMENT

	Basal insulin group	CSII group	P value
<i>n</i>	27	32	NS
FBG (mmol/L)			
After treatment	5.66 ± 1.09**	5.89 ± 1.22**	0.157
Change	−7.61 ± 3.72	−6.37 ± 3.93	0.222
2-h PBG (mmol/L)			
After treatment	10.2 ± 2.7*	6.2 ± 0.9**	< 0.001
Change	−9.1 ± 3.4	−11.1 ± 3.7	0.049
HbA _{1c} (%)			
After treatment	9.91 ± 1.95*	10.03 ± 1.91*	0.554
Change	−1.06 ± 0.66	−0.84 ± 0.57	0.196
Triglycerides (mmol/L) ^a			
After treatment	5.14 ± 0.92*	4.79 ± 0.75**	0.137
Change	−0.76 ± 0.82	−0.66 ± 0.62	0.638
Total cholesterol (mmol/L)			
After treatment	1.74 ± 0.83**	1.81 ± 0.65**	0.725
Change	−1.33 ± 1.57	−0.80 ± 0.97	0.143
LDL-C (mmol/L)			
After treatment	3.42 ± 0.68	3.09 ± 0.78*	0.198
Change	−0.12 ± 0.61	−0.47 ± 0.76	0.035
HDL-C (mmol/L)			
After treatment	1.17 ± 0.27	1.19 ± 0.59	0.886
Change	−0.07 ± 0.22	−0.04 ± 0.20	0.624
AIR (μIU/mL/min) ^a			
After treatment	6.75 ± 5.85	7.18 ± 12.94	0.202
Change	6.62 ± 6.78	8.27 ± 13.55	0.08
AUC _{Ins} (μIU/mL/min) ^a			
After treatment	205.22 ± 89.23**	205.30 ± 143.98**	0.998
Change	100.47 ± 91.66	90.41 ± 122.87	0.733
AUC _{Cpep} (pmol/mL/min) ^a			
After treatment	6.93 ± 1.84*	8.01 ± 2.72*	0.092
Change	0.71 ± 1.60	1.06 ± 1.18	0.350
HOMA-B ^a			
After treatment	164.3 ± 90.9**	141.9 ± 113.1**	0.412
Change	137.63 ± 87.38	101.52 ± 118.62	0.196
HOMA-IR ^a			
After treatment	3.59 ± 1.66**	3.85 ± 2.09**	0.593
Change	−2.44 ± 2.82	−2.83 ± 2.82	0.597
Days of achieving euglycemia (days)	5.4 ± 1.4	3.8 ± 1.9	0.002

Data are mean ± SD values unless otherwise indicated.

^aData are median ± interquartile values.

Compared with baseline, * $P < 0.05$, ** $P < 0.01$.

Compared between the two groups, P values are in boldface if there was a statistical difference.

AIR, acute insulin response; AUC_{Ins} and AUC_{Cpep}, area under the curve for insulin and C-peptide, respectively; BMI, body mass index; CSII, continuous subcutaneous insulin infusion; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HbA_{1c}, glycosylated hemoglobin; HOMA-B and HOMA-IR, β -cell function and insulin resistance, respectively, which were assessed by homeostasis model according to the equations HOMA-B = $(20 \times \text{fasting insulin}) / (\text{FPG} - 3.5)$ and HOMA-IR = $(\text{FPG} \times \text{fasting insulin}) / 22.5$; LDL-C, low-density lipoprotein cholesterol; NS, not significant; 2-h PBG, 2-h postprandial blood glucose.

The most commonly reported adverse events were hypoglycemic episodes. No severe hypoglycemic episodes, which were defined as an event requiring the assistance of another person, occurred during the intervention. A higher prevalence of minor hypoglycemic episodes or classical symptoms of hypoglycemia was observed in the CSII group (31.25% in CSII vs. 22.22% in the basal insulin group, $P < 0.05$), but the basal insulin group had a higher incidence of nocturnal hypoglycemia (11.11% vs. 3.13%, $P < 0.01$). About 56.25% of hypoglycemic episodes were asymptomatic and were detected by CGMS (60% in CSII vs. 50% in the basal insulin group). No obvious weight gain was observed in either group after insulin therapy. Mild injection site reactions (erythema, edema,

and pain) were observed, but there was no significant difference between the two groups.

Discussion

In the present study, we compared the effects of basal insulin monotherapy and CSII therapy in newly diagnosed T2DM patients. We found that after 2 weeks of short-term insulin therapy, 88.14% of patients achieved fasting glycemic control target, which was defined as fasting capillary blood glucose varying from 4.4 mmol/L to 6.0 mmol/L. The average postprandial plasma glucose concentrations also declined greatly in both groups, and HbA_{1c} decreased nearly 1%, with

FIG. 1. Dynamic changes of capillary blood glucose with time in two insulin treatment schemes: (A) fasting blood glucose (FBG) and (B) 2-h postprandial blood glucose (PBG). FBG levels compared between the two groups were not significantly different ($P > 0.05$); 2-h PBG levels compared between the two groups were significantly different (* $P < 0.05$, ** $P < 0.01$). CSII, continuous subcutaneous insulin infusion.

no significant difference between the two groups. Compared with those in the CSII group, patients in the basal insulin group achieved the same glycemic control and β -cell function restoration with a lower insulin dose. Moreover, their β -cell function, especially AIR, was greatly improved, irrespective of the use of CSII or basal insulin monotherapy. HOMA-B and HOMA-IR were also improved after short-term insulin intervention. These results are consistent with our previous study.¹¹

Basal insulin therapy is recommended to initiate insulin treatment in patients with T2DM whose glycemia is inadequately controlled by diet/exercise and OADs.^{15,16} Insulin glargine is a long-acting human insulin analog with a longer time-action profile and no pronounced peak of action compared with neutral protamine Hagedorn (NPH) insulin.^{17,18} In light of these advantages, insulin glargine has taken the place of NPH insulin for use as basal insulin. In this trial, we used it as monotherapy in newly diagnosed T2DM patients and compared its effect with CSII as the initial insulin therapy schema. We found basal insulin monotherapy and CSII had the same effects on fasting glycemic control and β -cell func-

tion improvement. We also found that the dose of insulin to reach the same end point was lower in basal insulin monotherapy. Moreover, it is more convenient to use—especially in outpatients, who have more psychological resistance to insulin (which is the greatest obstacle to the initiation of insulin).^{12,19}

The advantage of insulin treatment on glycemic control and β -cell function improvement in diabetes has been fully confirmed.^{7–11,20} All those trials used CSII or multiple daily insulin injections as initial insulin intervention and attributed the recovery of β -cell function to insulin replacement allowing β -cell rest. Considering the importance of insulin treatment and FPG, each of which has a close relationship with the first-phase insulin secretion, in the present study we used only basal insulin as supplement monotherapy and only controlled fasting blood glucose levels. We found the same effect on the improvement of β -cell function and glycemic control. This observation suggests again that the damage to β -cell function in newly diagnosed T2DM patients can be reversible through any kind of early glycemic control by insulin, whether it is CSII, multiple daily insulin injections, or basal insulin

FIG. 2. Changes in (A) plasma fasting insulin and (B) C-peptide during intravenous glucose tolerance test before and after insulin treatment. Both groups' plasma fasting insulin and C-peptide levels were elevated after insulin treatment, compared with before ($P < 0.05$), and there was no statistical difference between the two groups ($P > 0.05$). CSII, continuous subcutaneous insulin infusion.

FIG. 3. (A) Area under the curve for insulin (AUC_{ins}), (B) area under the curve for C-peptide ($\text{AUC}_{\text{C}_{\text{pep}}}$), and (C) acute insulin response (AIR) in the two groups before and after insulin therapy. $P < 0.01$ before versus after insulin therapy in each group, $P > 0.05$ between the two groups both before and after insulin therapy.

monotherapy. It is notable that the plasma lipid profile and HOMA-IR were also improved after short-term insulin therapy without using lipid-adjusting agents. Glucolipotoxicity generated by hyperglycemia and related pathogenesis factors can damage β -cell function. By eliminating these damaging effects, early insulin therapy could reduce β -cell stress, improve endogenous insulin processing, and restore the injured β -cells' function.^{2,3,21} Obviously, the metabolic effect of any basal insulin preparation on fasting blood glucose level is supported by endogenous insulin secretion in individuals with T2DM. In addition, insulin glargine reduced β -cell stress more effectively because of its longer-lasting pharmacodynamic profile.²² Other insulin effects such as reducing inflammation and decreasing ectopic lipid deposition might

also contribute to the recovery of overall β -cell function in T2DM patients.^{23,24}

In addition, our results indicated that fasting blood glucose level was the main risk factor affecting β -cell function. In vitro experiments have shown that the first-phase insulin secretion of β -cells was damaged or vanished when the fasting blood glucose level was above 97 or 100 mg/dL, respectively.^{25,26} With the increasing of fasting blood glucose levels, β -cell mass decreases.²⁷ Tfayli et al.²⁸ observed a total of 223 youths with $\text{FPG} < 126$ mg/dL who underwent evaluation of first- and second-phase insulin secretion during a 2-h hyperglycemic clamp and found that the impairment in β -cell function relative to insulin sensitivity was apparent even within the FPG range of those without diabetes; at the current cutoff of 100 mg/dL for impaired fasting glucose, there is an approximately 49% decline in the glucose disposition index.²⁸ Subsequently, some experts have suggested that the target of fasting blood glucose control should be less than 100 mg/dL.

The present study does, however, have some limitations that need to be discussed. First, this was a short-term open-label study, and the favorable clinical benefits observed in this trial should be tested through long-term follow-up studies. Second, this was an observational study that had relatively straightforward aims; in this trial, we primarily paid attention to the patients' fasting blood glucose and less so to their postprandial blood glucose levels, whereas strict clinical guidelines would stipulate giving equal attention to both. Third, the results only apply to lean patients with T2DM with poor baseline glycemic control because the β -cell function of

TABLE 3. INSULIN DOSE IN EACH GROUP

Insulin dose	Basal insulin group	CSII group	P value
Maximum daily			
IU	42.7 ± 10.2	59.3 ± 17.1	0.001
IU/kg	0.66 ± 0.15	0.89 ± 0.26	0.003
Final daily			
IU	35.5 ± 10.9	48.1 ± 17.5	0.009
IU/kg	0.55 ± 0.21	0.72 ± 0.31	0.025
Total			
IU daily	38.6 ± 10.5	54.7 ± 17.3	0.002
IU/kg	0.59 ± 0.18	0.81 ± 0.29	0.007

CSII, continuous subcutaneous insulin infusion.

these patients exhibits obvious deterioration and insulin therapy can provide β -cell rest. However, in obese and mild T2DM patients, the most important concern is insulin resistance, so drugs that can improve insulin resistance, such as metformin, might be more suitable for them. Despite all these limitations, the significance of this study should not be ignored. The results suggest that basal insulin monotherapy could have similar effects to CSII. And, considering its importance and limitations, the results of this study should be reproducible in the vast majority of T2DM patients with similar characteristics.

In summary, compared with CSII, basal insulin monotherapy had a similar effect on glycemic control and β -cell function improvement in newly diagnosed T2DM patients. Therefore basal insulin monotherapy might be a reasonable alternative to CSII for initial insulin therapy in newly diagnosed T2DM patients.

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Author Disclosure Statement

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