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Needle-free jet injection of insulin glargine improves glycaemic control in patients with type 2 diabetes mellitus: a study based on the flash glucose monitoring system

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7 **glycaemic control in patients with type 2 diabetes mellitus:**
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Abstract

Background: Needle-free jet injection of insulin has faster subcutaneous absorption than that when using an insulin pen. The aim of this study was to investigate the effects of insulin glargine injection given with a QS-P jet injector on the glucose profile using a professional mode flash glucose monitoring (FGM) system in patients with type 2 diabetes mellitus (T2DM).

Research design and methods: In this randomized, controlled, cross-sectional study, 66 patients with T2DM who received insulin glargine (12–18 IU/day) injection were enrolled. The patients were randomly divided into group A (jet injector before insulin pen) and group B (insulin pen before jet injector). Each subject injected insulin daily before breakfast. We analyzed the changes in the glucose profile using a professional mode FGM system.

Results: Treatment with a jet injector led to significantly lower 24-h mean glucose, maximum blood glucose, area under the curve (AUC) >10.0 mmol/L, time above range and increased AUC < 3.9 mmol/L and time below range than those when using an insulin pen. There was no difference in glycemic variability between the two groups. We observed that patients using a jet injector had significantly lower mean glucose between 12:00 to 22:00.

Conclusions: Needle-free jet injection of insulin glargine was more effective than use of an insulin pen for good glycemic control in patients with T2DM.

Keywords: Needle-free jet injector, insulin glargine, insulin pen, flash glucose monitoring system, type 2 diabetes mellitus

Clinical trial registration: www.clinicaltrials.gov identifier is NCT04093284

Article highlights

- This study aimed to investigate the effects of insulin glargine administered using a QS-P jet injector on the glucose profile and safety in patients with T2DM.
- The 24-h mean glucose was significantly lower in the jet injector group than in the insulin pen group.
- There was a significant improvement in glycemic control when insulin glargine was administered using a jet injector.
- Patients using a jet injector had significantly lower mean glucose levels from 12:00 to 22:00 compared to those using an insulin pen.
- The risk of hypoglycemia was higher in the jet injector group.
- There was no significant difference in operation convenience, satisfaction, acceptance, or injection pain scores.

1. Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is growing significantly worldwide, especially in developing countries[1]. China ranks first with the highest number of patients with diabetes [2,3]. Although there are various therapeutic patterns for T2DM, only less than half of the patients had adequate glycemic targets in China [2,4]. In patients with T2DM, poor glycemic control can lead to worse outcomes, including more complications, higher medication costs, and higher hospitalization rates and mortality [5-7]. Prevention strategies and good glycemic control in patients tend to improve outcomes and decrease the economic effect of T2DM.

According to the guidelines for T2DM published by the Chinese Diabetes Society, insulin therapy is currently considered a therapeutic option for patients in whom

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4 blood glucose levels are not adequately controlled using diet/exercise and oral
5 medications [2]. Approximately 50% of the Chinese population with T2DM receives
6 insulin treatment [8]. The effect of and adherence to insulin treatment are influenced
7 by the insulin delivery device. It was found that insulin pen devices were shown to
8 offer better persistence and adherence than insulin vial-and-syringe delivery [9].
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10 When using needle injection therapy, injection-related anxiety, the complexity of
11 treatment options and subcutaneous allergy and induration will affect insulin
12 treatment and patient compliance, resulting in a failure to reach glycemic targets with
13 insulin analogs [10,11].
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22 Since the discovery of insulin, great efforts have been made to develop effective
23 needle-free insulin delivery technology worldwide. The insulin pens inject insulin into
24 the subcutaneous tissue through needles, which involve skin penetration. Insulin
25 administration using jet injectors, which provide a needle-free alternative to insulin
26 pens, are already available for clinical application. The jet injector pushes insulin in a
27 drug tube at high velocity (typically >100 m/s) across the skin, dispensing it over a
28 larger subcutaneous area than insulin injected with a needle [12]. Due to the lack of
29 needles, this technique provides little stimulation of subcutaneous nervous tissue,
30 produces a weak stinging sensation, and the drug solution can be absorbed diffusely
31 under the skin, close to the mode of human insulin secretion. The body absorbs the
32 insulin more quickly, and the insulin works faster. Patients with T2DM treated with
33 rapid-acting insulin using jet injection had a significantly shorter onset time of insulin
34 and significantly improved early postprandial glucose control compared with those
35 when using insulin pens [13,14]. Compared with traditional needle injection, this jet
36 injection has irreplaceable technical advantages.
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52 The QS-P injector (Beijing QS Medical Technology Co. Ltd, China), a new
53 generation of syringe without a needle, is specially designed for insulin injection in
54 patients with diabetes. It can take an injectable dose of 4–35 units for a single
55 injection. The new QS-P injector is more convenient to use than the old model (QS-
56 M injector). It takes only three steps for the QS-P injector to inject insulin and four
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4 steps for the QS-M injector. Compared with the QS-M injector, the QS-P injector is
5 lighter (95 g vs. 220 g), shorter in length (15 cm vs. 19.5 cm), and faster in jet
6 velocity (200–220 m/s vs. 180–200 m/s). In addition, the injection sound of the QS-P
7 injector is quieter than that of the QS-M injector. Previous studies have shown that
8 the use of the QS-M injector can lower the dosage of insulin required to achieve
9 good glycemic control in patients with T2DM [15,16]. However, few studies have
10 specifically addressed the glycemic effect of the QS-P injector on basal insulin in
11 T2DM.
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20 At present, using a professional mode flash glucose monitoring (FGM) system,
21 with data masked from users until retrieved by healthcare professionals, could
22 provide the glycemic profiles necessary for professionals to personalize treatment
23 [17]. The aim of the current study was to investigate the effects of subcutaneous
24 insulin glargine injection using a QS-P needle-free jet injector and conventional pen
25 on the blood glucose profile and safety using a professional mode FGM system in
26 patients with T2DM.
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35 **2. Patients and methods**

36 **2.1 Study population**

37 This randomized, controlled, crossover, single-center study was conducted at the
38 Endocrinology Department of Nanjing First Hospital, Nanjing Medical University,
39 China. The patient inclusion criteria were as follows: volunteered to participate and
40 provided signed informed consent prior to the trial; patients aged 18–65 years with a
41 body mass index (BMI) 18–30 kg/m² and diagnosis of T2DM (meeting the WHO1999
42 diagnostic criteria) for more than half a year; patients receiving a stable insulin
43 glargine (100 U/ml) dosage of 12 to 18 IU daily, single insulin or combined with oral
44 antidiabetics, and all drug doses were stable for more than 2 months; subjects were
45 able and willing to monitor peripheral blood sugar and regularity of diet and exercise;
46 and no acute complications, such as diabetic ketoacidosis, diabetic hyperosmolar
47 syndrome, repeated hypoglycemia. The exclusion criteria were as follows: patients
48 with insulin allergy; patients with impaired liver and kidney function with a plasma
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alanine transferase (ALT) level 2.5 times higher than the upper limit of the normal value; serum creatinine was 1.3 times higher than the upper limit of normal; a history of drug abuse and alcohol dependence in the past 5 years; systemic hormone therapy was used in the last 3 months; patients with poor compliance and irregular diet and exercise; patients who were pregnant, lactating, or intended to become pregnant; skin diseases such as exfoliative dermatitis; treatment with anticoagulants and/or immunosuppressants; and any other obvious conditions or associated diseases determined by the researcher.

This study was approved by the Ethics Committee of Nanjing First Hospital. All procedures followed were in accordance with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for inclusion in this study. It was registered at ClinicalTrial.gov with registration number NCT04093284.

2.2 Study design

In this study, 66 patients with T2DM who received abdominal subcutaneous insulin glargine injection were enrolled. One patient withdrew consent, two patients experienced probe shedding, the insulin dosage was adjusted in four patients due to the symptomatic hypoglycemia, and complete data were not obtained from two patients; finally, 57 patients completed the study. The study design and flowchart of patients in the trial are shown in Figure 1.

The study lasted for 17 days. All patients received a standardized diet, which was designed to ensure a total energy intake of 20–30 kcal/kg per day consisting of 55% of energy from carbohydrates. They were also required to refrain from both structured and recreational physical activities. There was no change in the type or dosage of medication taken by the patients before enrollment and during this study. All subjects were administered insulin glargine (Basalin, CN) daily before breakfast (07:00), and an abdominal subcutaneous injection site was selected.

The patients were randomly divided into group A (jet injector during days 1–8, then

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4 crossover to insulin pen during days 9–17) and group B (insulin pen during days 1–8,
5 then crossover to jet injector during days 9–17). During the 4-day washout period
6 (days 1–4 or days 9–12), the same specialist instructed all patients how to master
7 the injection techniques daily, so that they were proficient with both the QS-P jet
8 injector and conventional insulin pen injections. All participants wore a FreeStyle
9 Libre sensor for FGM from day 4 to day 17.
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15 16 **2.3 The FGM system**

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18 The FreeStyle Libre professional-mode FGM system (Abbott Diabetes Care, UK)
19 has three components: a disposable sensor (worn for up to 14 days), a handheld
20 reader retained by the health professional, and associated software. The sensor was
21 applied at the clinic to the upper arm of the participants. Over the 14-day period, the
22 sensor recorded interstitial glucose concentrations every 15 min, but the glucose
23 data were not available to the patients until their scheduled visit when a health
24 professional uploaded their data to a computer via the reader. After completion of the
25 FGM intervention, the glucose data were downloaded. We analyzed the FGM data
26 from day 5 to day 8, together with that from day 13 to day 16.
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37 The following glycemic variability indices obtained from the FGM were calculated:
38 24-h mean blood glucose (MBG) (defined as the average glucose of 96
39 measurements equally spaced in time), mean amplitude of glycemic excursion
40 (MAGE), standard deviation of mean glucose (SDBG), and coefficient of variation
41 (CV %). The incremental area under the curve (AUC) of the glucose level > 10.0
42 mmol/L and area over the curve (AOC) of a glucose level < 3.9 mmol/L were
43 calculated using the trapezoid rule. Time in rang (TIR, glucose level 3.9–10.0
44 mmol/L), time above rang (TAR, glucose level > 10.0 mmol/L), and time below rang
45 (TBR, glucose level < 3.9 mmol/L) were also calculated.
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55 56 **2.4 Clinical and laboratory examination**

57 Patient data, including demographic characteristics, lifestyle habits, medical
58 history and medication use, were obtained using a standard questionnaire. Height
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and body weight were measured using a digital scale, and BMI was calculated as weight divided by height squared (kg/m^2).

Blood samples were collected after the patients fasted overnight (≥ 8 hours). Biochemical parameters, including fasting blood glucose (FBG), ALT, aspartate aminotransferase (AST), total cholesterol (TC), triglyceride (TG), and serum creatinine (SCr) were measured using routine laboratory methods using a HITACHI 7600 device (HITACHI, Tokyo, Japan). The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation: $\text{eGFR (mL}/\text{min}/1.73 \text{ m}^2) = 186 \times (\text{SCr}/88.4)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female})$.

2.5 Assessment of safety and tolerance

Before and after the study, a questionnaire was provided to each patient to assess the acceptability and the tolerance of using the QS-P jet injector and glargine pen. The form included a few short-answer questions regarding operation convenience, satisfaction, acceptance, and skin injuries (bruise, redness, and infection). Injection-associated pain score was rated from 0 (no pain) to 7 (worst pain imaginable).

2.6 Statistical analysis

All statistical analyses were performed using SPSS 17.0 for Windows (Chicago, IL, USA). Data are reported as mean \pm standard deviation (SD) for normally distributed continuous variables and median with interquartile range for non-normally distributed continuous variables. Comparisons between groups were made using Student's paired t-test for normally distributed continuous variables. Non-normally distributed continuous parameters were analyzed using non-parametric tests. A p -value of less than 0.05 was considered statistically significant.

3. Results

A total of 57 patients (37 men and 20 women, with a mean age of 54.69 ± 6.82 years) with T2DM successfully completed this study. Their daily dose of insulin was 14.13 ± 1.98 units, with a BMI of $24.82 \pm 2.74 \text{ kg}/\text{m}^2$, FBG of $8.33 \pm 2.22 \text{ mmol}/\text{L}$,

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4 and GA of 19.21% (15.91–22.02 %). The clinical and laboratory characteristics of
5 subjects are described in Table 1.
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9 Table 2 shows the glucose fluctuation variables measured using an FGM for
10 insulin administration with the needle-free jet injector and insulin pen. The 24-h MBG
11 was significantly lower with the jet injector than with the insulin pen (8.67 ± 2.22 vs.
12 9.11 ± 2.58 mmol/L, $p=0.004$). A difference was also seen in the MaxBG (16.15 ± 3.17
13 vs. 16.79 ± 3.49 mmol/L, $p=0.032$). There was no significant difference in glycemic
14 variability parameters (MAGE, SDBG, or CV %) between the two groups.
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21 In contrast to the insulin pen, treatment with the jet injector decreased the AUC for
22 blood glucose >10.0 mmol/L [82.54 (13.80, 110.20) vs. 109.27 (16.67, 136.41)
23 mmol/L·hour, $p=0.034$] and the TAR [29.65 (13.50, 41.67) vs. 33.11 (13.54,
24 49.89) %, $p=0.046$]. Treatment with the jet injector resulted in a decrease in the level
25 of hyperglycemia. Insulin glargine administration using the jet injector increased the
26 AUC of blood glucose <3.9 mmol/L ($p=0.008$) and TBR ($p=0.008$).
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34 The average blood glucose concentration per hour measured using the FGM in
35 patients after administration of insulin glargine with a jet injector or insulin pen is
36 shown in Fig. 2. We observed that patients using a jet injector had significantly lower
37 mean glucose levels from 12:00 to 22:00 than those using an insulin pen ($p<0.05$).
38 Therefore, the lower 24-h MBG when using a jet injector mainly depended on the
39 decrease in postprandial glucose.
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48 Glucose fluctuation-related variables from 12:00 to 24:00 were examined in
49 patients who received insulin administration via a jet injector or conventional insulin
50 pen. The results are shown in Table 3. The 12-h MBG was significantly lower with jet
51 injector use than with insulin pen use (9.06 ± 2.16 vs. 9.72 ± 2.73 mmol/L, $p=0.003$).
52 Differences were also seen in the MaxBG (15.13 ± 3.28 vs. 15.93 ± 3.65 mmol/L,
53 $p=0.021$) and MinBG [4.22 (3.20, 5.05) vs. 4.86 (3.55, 5.10) mmol/L, $p=0.003$]. In
54 contrast to the insulin pen, treatment with a jet injector decreased the 12-h AUC of
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4 blood glucose >10.0 mmol/L [45.53 (8.58, 56.30) vs. 66.13 (8.29, 91.61)
5 mmol/L*hour, $p=0.009$] and increased the 12-h AUC of blood glucose <3.9 mmol/L
6 [0.93 (0.00, 0.72) vs. 0.34 (0.00, 0.11) mmol/L*hour, $p=0.009$]. However, there was
7 no difference in the 12-h TIR, TAR, or TBR between the two treatment methods
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11 ($p>0.05$).
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14 Before the study, the questionnaire survey revealed that 31.6% of patients were
15 willing to use insulin pen treatment, while 68.4% of the patients preferred to choose
16 jet injector treatment. However, only 36.8% of the patients preferred the jet injector
17 after finishing this study, while 63.2% of the patients decided to continue using an
18 insulin pen. During the research period, there were no serious adverse events,
19 redness, or infection at the abdominal injection site. Two patients (3.5%) in group B
20 had bruising at the injection site when using the QS-P jet injector. One patient in
21 group A and one patient in group B had bruising at the injection site when using an
22 insulin pen. Once skin bruises appeared in the patient, there was no similar situation
23 after changing the insulin site from the following injection. There was no significant
24 difference in operation convenience, satisfaction, acceptance, or injection pain
25 scores (mean scores, 2.63 ± 1.29 for jet injector vs. 2.85 ± 1.64 for conventional pen,
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 $p=0.43$).

4. Discussion

This was a randomized, controlled, crossover study, to investigate the effects of subcutaneous basal insulin injection with a QS-P needle-free jet injector and conventional insulin pen on glucose profile and safety in patients with T2DM. We observed significantly improved glycemic control when insulin glargine was administered using a QS-P jet injector compared with that when using an insulin pen at the same insulin dose in T2DM patients. This study provides evidence to support the application of needle-free injection in Chinese patients with T2DM.

Previously, we showed that insulin glargine delivered by a QS-M injector led to a potential improvement in lowering mean glucose levels in patients with T2DM [18]. In

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4 the current study, we found that the MaxBG, AUC of glucose >10.0 mmol/L, and
5 TAR were significantly lower when using the QS-P jet injector than when using the
6 insulin pen. These results indicate that the jet injector is more effective than the
7 insulin pen in reducing the risk of hyperglycemia. The jet injects insulin through the
8 insulin pen in reducing the risk of hyperglycemia. The jet injects insulin through the
9 skin by forcing a high-pressure liquid flow, which can spread out more in the
10 subcutaneous layer of the skin than when using the pen [19]. This method of insulin
11 administration significantly accelerates the absorption of rapid-acting insulin from the
12 subcutaneous tissue into the systemic circulation in both healthy volunteers and
13 patients with diabetes [14,20]. Previous studies showed that jet injection accelerated
14 the absorption of insulin aspart and was followed by a reduction in early postprandial
15 hyperglycemia in patients with diabetes [13,14,21]. Therefore, it was reasonable to
16 consider that the observed glycemic effects might be related to the faster absorption
17 of insulin glargine when using the QS-P jet injector than when using the insulin pen.
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30 Using the jet injector group led to significantly lower mean glucose levels from
31 12:00 to 22:00 compared to those when using the conventional insulin pen. Use of
32 the jet injector and pen injections produced similar FBG levels. This underlying
33 mechanism may be explained first by the administration of insulin glargine before
34 breakfast (07:00). Insulin glargine is a long-acting insulin analog with well-
35 established efficacy and safety profiles, with an onset time of 4 hours following
36 subcutaneous injection [22,23]. The use of the needle-free jet injector treatment
37 could increase the absorption rate of insulin glargine resulting in a faster onset of
38 action. Second, patients included in this study had a small dose of insulin at 12–18
39 IU daily. There was no subcutaneous allergy or induration at the injection site on the
40 abdominal skin. Therefore, the total absorption of insulin remained unchanged or
41 changed slightly. Engwerda et al. reported that there were no differences in the
42 variability of the efficacy endpoints between the jet injector and routine insulin pen
43 administration [24]. Because the daily dose of insulin was constant, there was no
44 difference in FBG between the two treatment methods.
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Accompanied by the decrease in hyperglycemia, our results indicated that the risk

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4 of hypoglycemia also increased in the jet injector group. It has been reported that the
5 use of a needle-free injector reduced the insulin dosage required for good glycaemic
6 control in patients with T2DM [15,16]. Moreover, the degree of insulin reduction with
7 jet injection was positively correlated with insulin dosage [16]. In addition, we also
8 noted that four patients dropped out of the study after adjusting the insulin dosage.
9 The survey feedback revealed that these four patients reduced their insulin dosage
10 because of symptomatic hypoglycemia. These findings support that the jet injector
11 could reduce the dose of basal insulin in patients with T2DM, thereby reducing the
12 risks of high-dose insulin therapy and the financial burden on patients.
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22 The results of the survey feedback indicated that most patients preferred the
23 conventional insulin pen over the jet injector. However, the jet injector and insulin
24 pen showed similar levels of patient convenience for operation, satisfaction,
25 acceptance and injection pain scores. The patient preference might be related to the
26 short period over which the jet injector was used. In addition, the patients in this
27 study generally tolerated insulin pen injections without obvious discomfort,
28 consequently feeling no need to change the mode of injection. Future studies are
29 necessary to reveal the tolerability of the jet injector after personal experience in
30 daily clinical practice for sufficient duration.
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41 Some limitations of this study must be addressed. First, we did not investigate the
42 pharmacology of insulin glargine administered using a needle-free jet injector versus
43 an insulin pen. Second, the observation period is relatively short, because the
44 treatment of diabetes is a long-term process. Finally, this was not a double-blind
45 study. We could not exclude possible bias induced by the recognition of the insulin
46 injection method.
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52 53 **5. Conclusion**

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55 In conclusion, our study indicated that the QS-P jet injector was more effective
56 than the conventional insulin pen in achieving strict glycaemic control in T2DM
57 patients using insulin glargine. This observed improvement in glycaemic control
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4 mainly manifested as a significant improvement of the 24-h MBG, especially in the
5 mean glucose levels from 12:00 to 22:00. Meanwhile, it might be necessary to
6 reduce the insulin glargine dosage when using a needle free syringe instead of an
7 insulin pen to avoid hypoglycemia in diabetic patients.
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28 **Declaration of interest**

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31 The authors have no relevant affiliations or financial involvement with any
32 organization or entity with a financial interest in or financial conflict with the subject
33 matter or materials discussed in the manuscript. This includes employment,
34 consultancies, honoraria, stock ownership or options, expert testimony, grants or
35 patents received or pending, or royalties.
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45 **Reviewer disclosures**

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47 A reviewer on this manuscript has disclosed that they are a scientific founder and
48 minor stockholder of Portal Instruments, Inc. The company is not currently working in
49 insulin delivery for diabetes management and the reviewer has no ongoing
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Legends

Figure 1 Study design and the flow of patients in the study. JI (jet injector); IP (Insulin pen).

Figure 2 The 24h FGM glucose fluctuation profile of patients using jet injector or insulin pen. * $p < 0.05$, # $p < 0.01$.

Table 1 Clinical and laboratory characteristics of the participants.

Table 2 Glucose fluctuation parameters for insulin administration with the jet injector and insulin pen.

Table 3 Glucose fluctuation parameters of 12:00-24:00 (12h) for insulin administration with the jet injector and insulin pen.

Table 1 Clinical and laboratory characteristics of the participants.

Characteristics	Whole group (n=57)	Characteristics	Whole group (n=57)
Male-to-female ratio	37/20	BMI (kg/m ²)	24.82 ± 2.74
Age (years)	54.69 ± 6.82	Waist-hip ratio (cm/cm)	0.96 (0.93, 1.01)
Duration of diabetes (years)	9.47 ± 6.17	SBP (mmHg)	136.60 ± 18.00
Daily of insulin dose (units)	14.13 ± 1.98	DBP (mmHg)	87.06 ± 10.51
History of hypertension (n(%))	28 (48.28%)	FBG (mmol/L)	8.33 ± 2.22
History of CVD (n(%))	7 (12.07%)	GA (%)	19.21 (15.91, 22.02)
Diabetic microangiopathy (n(%))	6 (10.34%)	ALT (U/L)	17.46 (10.93, 20.68)
DPN (n(%))	1 (1.72%)	AST (U/L)	23.85 (18.98, 27.63)
Family history of T2DM (n(%))	16 (27.59%)	TC (mmol/L)	4.30 ± 0.89
Use of antiplatelet drugs (n(%))	10 (17.24%)	TG (mmol/L)	1.54 (0.86, 1.97)
Use of statins (n(%))	9 (15.52%)	SCr (□mol/L)	61.50 ± 15.16
Use of metformin (n(%))	30 (51.72%)	eGFR (ml/min/1.73m ²)	120.35 ± 26.76

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5 Values are presented as means \pm SD, or median (25th – 75th range), or numbers (%).

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7 Abbreviations: CVD, Cardiovascular disease; DPN, Diabetic peripheral neuropathy; BMI, body mass
8 index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; GA,
9 glycated albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TC, total
10 cholesterol; TG, triglyceride; SCr, serum creatinine; eGFR, estimated glomerular filtration rate.
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Table 2 Glucose fluctuation parameters for insulin administration with the jet injector and insulin pen

Parameters	Jet injector	Insulin pen	<i>P</i> value
24-h MBG (mmol/L)	8.67 ± 2.22	9.11 ± 2.58	0.004
MAGE (mmol/L)	7.46 ± 3.14	7.53 ± 2.60	0.858
SDBG (mmol/L)	2.43 ± 0.60	2.55 ± 0.68	0.061
CV %	0.29 ± 0.07	0.29 ± 0.06	0.829
MaxBG (mmol/L)	16.15 ± 3.17	16.79 ± 3.49	0.032
MinBG (mmol/L)	3.91 ± 1.47	4.31 ± 2.01	0.056
AUC > 10.0mmol/L	82.54 (13.80, 110.20)	109.27 (16.67, 136.41)	0.034
AUC 3.9-10mmol/L	371.77 (304.91, 499.5)	379.10 (313.64, 449.01)	0.319
AOC < 3.9mmol/L	2.85 (0.00, 1.31)	1.43 (0.00, 0.79)	0.008
TAR (%)	29.65 (13.50, 41.67)	33.11 (13.54, 49.89)	0.046
TIR (%)	65.70 (55.08, 81.57)	64.22 (46.96, 83.85)	0.487
TBR (%)	4.64 (0.00, 4.04)	2.67 (0.00, 2.34)	0.008

Values are presented as means ± SD, or median (25th – 75th range).

24-h MBG: 24 hr mean glucose (mmol/L); MAGE: mean amplitude of glycemic excursions (mmol/L); SDMG: standard deviation (mmol/L); CV%: the coefficient of variation; MaxBG: maximum blood glucose (mmol/L); MinBG: minimum blood glucose (mmol/L); AUC > 10.0 mmol/L: the incremental area under the curve (AUC) of glucose >10.0 mmol/L (mmol/L*hour); AOC < 3.9 mmol/L: the incremental area over the curve (AOC) of plasma glucose < 3.9 mmol/L (mmol/L*hour); AUC 3.9-10.0 mmol/L: the incremental AUC of glucose levels between 3.9 and 10 mmol/L (mmol/L*hour); TAR : time above

range (%); TIR : time in range (%); TBR : time below range (%).

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Table 3 Glucose fluctuation parameters of 12:00-24:00 (12-h) for insulin

Parameters	Jet injector	Insulin pen	<i>P</i> value
12-h MBG (mmol/L)	9.06 ± 2.16	9.72 ± 2.73	0.003
12-h MaxBG (mmol/L)	15.13 ± 3.28	15.93 ± 3.65	0.021
12-h MinBG (mmol/L)	4.22 (3.20, 5.05)	4.86 (3.55, 5.10)	0.003
12-h AUC > 10.0mmol/L	45.53 (8.58, 56.30)	66.13 (8.29, 91.61)	0.009
12-h AUC 3.9-10.0mmol/L	201.73(179.26, 236)	209.59 (175.58, 247.15)	0.068
12-h AOC < 3.9 mmol/L	0.93 (0.00, 0.72)	0.34 (0.00, 0.11)	0.009
12-h TIR (%)	61.97 (46.88, 80.21)	60.38 (45.05, 82.55)	0.749
12-h TAR (%)	35.83 (16.67, 52.60)	36.95 (13.80, 54.95)	0.715
12-h TBR (%)	2.20 (0.00, 2.34)	2.67 (0.00, 2.60)	0.832

administration with the jet injector and insulin pen

Values are presented as means ± SD, or median (25th – 75th range).

12-h MBG: 12 hr mean glucose (mmol/L); MaxBG: maximum blood glucose (mmol/L); MinBG: minimum blood glucose (mmol/L); AUC > 10.0mmol/L: the incremental area under the curve (AUC) of glucose >10.0 mmol/L (mmol/L*hour); AUC 3.9-10.0 the incremental AUC of glucose levels between 3.9 and 10.0 mmol/L (mmol/L*hour); AOC < 3.9 mmol/L: the incremental area over the curve (AOC) of plasma glucose < 3.9 mmol/L (mmol/L*hour); TIR: time in range (%); TAR: time above range (%); TBR: time below range (%).

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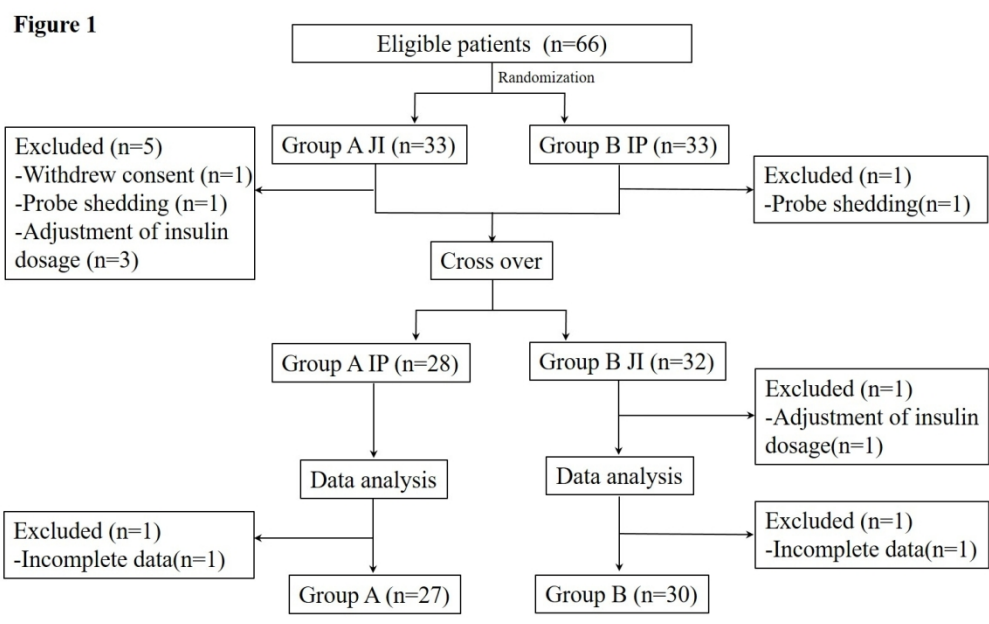


Figure 1 Study design and the flow of patients in the study. JI (jet injector); IP (Insulin pen).

268x167mm (150 x 150 DPI)

Figure 2

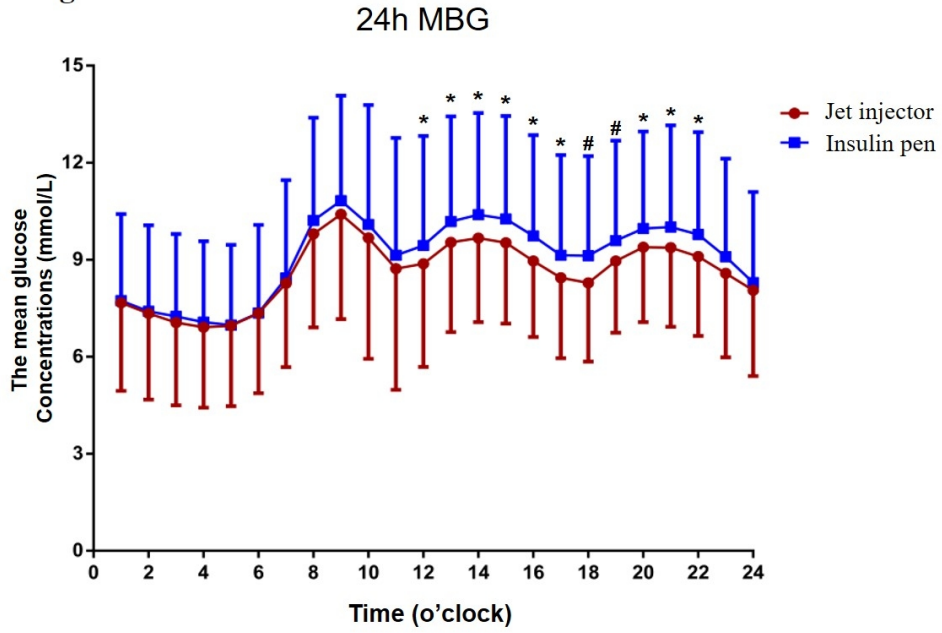


Figure 2 The 24h FGM glucose fluctuation profile of patients using jet injector or insulin pen. *p<0.05, #p<0.01.

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