A Feasibility Study of a 3-Day Basal-Bolus Insulin Delivery Device in Individuals With Type 2 Diabetes

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OBJECTIVE

This study tested the feasibility of transition from multiple daily injections (MDI) to a 3-day, basal-bolus insulin delivery device (PaQ) for type 2 diabetes (T2D).

RESEARCH DESIGN AND METHODS

Twenty MDI-treated individuals with T2D with HbA_{1c} ≤9% (75 mmol/mol) were enrolled in a single-center, single-arm pilot study, lasting three 2-week periods: baseline (MDI), transition to PaQ, and PaQ therapy. Feasibility of use, glycemic control, safety, and patient satisfaction were assessed.

RESULTS

Nineteen participants transitioned to PaQ treatment and demonstrated competency in assembling, placing, and using the device. Self-monitored blood glucose and blinded continuous glucose-monitoring data showed glycemic control similar to MDI. Study participants reported high satisfaction and device acceptance.

CONCLUSIONS

PaQ treatment is both feasible and acceptable in individuals with T2D. Transition from MDI is easy and safe. PaQ treatment might lead to better therapy adherence and improvements in glycemic control and clinical outcomes.

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Continuous subcutaneous insulin infusion has the potential to improve glycemic control and quality of life in individuals with type 2 diabetes (T2D) (1–6) but is not widely used in this population due to cost, device complexity, and extensive training requirements (7). Although currently available insulin pumps can be programmed to deliver up to 48 different basal rates per day, data from recent studies show good glycemic control in T2D by using only one or two daily basal rates (6,8). We tested a new, small, and discreet insulin delivery device (PaQ; CeQur SA, Horw, Switzerland) specifically designed for individuals with T2D. PaQ is directly applied to the skin, and insulin is infused at a constant basal rate for 3 days at one of five preset basal rates (Fig. 1*A* and *B*).

RESEARCH DESIGN AND METHODS

This 6-week, prospective, single-arm, single-center pilot study evaluated the feasibility of using PaQ in individuals with T2D currently treated with multiple daily injections (MDI). The study comprised three, two-week study periods: baseline (MDI), transition from MDI to PaQ, and PaQ treatment.

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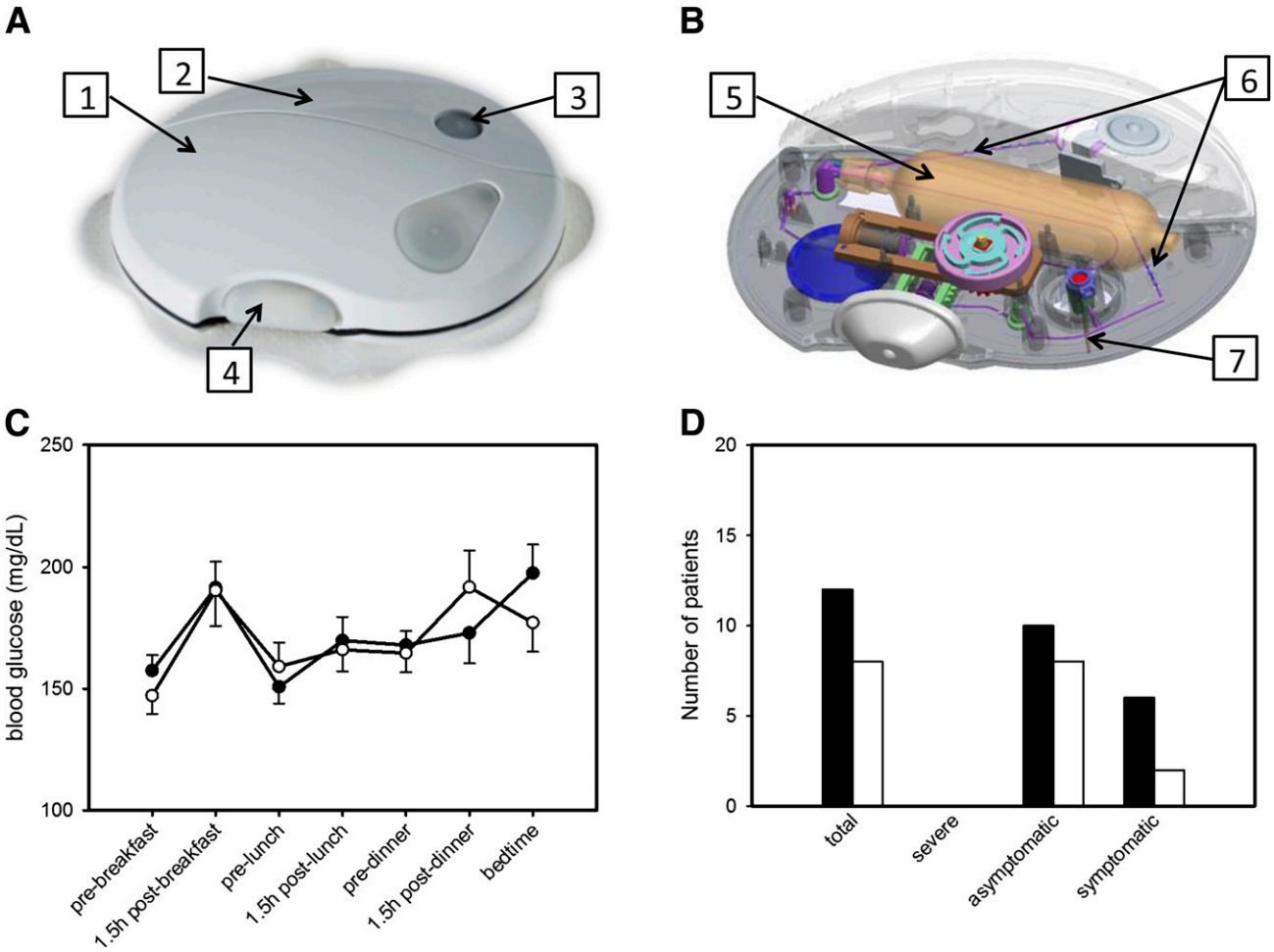

Figure 1—A: PaQ is a small (50 mm × 70 mm × 17 mm), 3-day insulin delivery device that is applied directly to the skin. Insulin reservoir (disposable): available with five preset basal rates (20, 24, 32, 40, and 50 U/24 h) (1). Messenger unit: reusable over 3 months, emits vibrations (2). Status button: informs the user how long the PaQ has been worn and when to change (3). Bolus button: each push delivers 2 U of insulin (4). B: Internal components of PaQ. Elastomeric bladder that drives basal flow (5). Capillary flow restrictors that control the basal rate (6). Cannula (8 mm) (7). C: Seven-point glucose profiles (mean ± SEM) during baseline period (black circles) and PaQ treatment (white circles). D: Number of patients experiencing hypoglycemic events during baseline period (black columns) and PaQ treatment (white columns).

The primary objective of this study was to evaluate participants' ability to use PaQ. A yes/no questionnaire was completed to evaluate each participant's ability to assemble, fill, prime, and apply PaQ, insert the cannula, administer bolus doses, and change the reservoir. In addition, understanding the signals emitted from PaQ and the action to be taken in response were also assessed.

Secondary objectives included:

- The transition from MDI to PaQ by the number of PaQ basal dose adjustments needed to maintain fasting glycemic control, total daily insulin dose (TDD), and number of meal boluses;
- The effectiveness of PaQ to maintain glycemic control by seven-point self-monitoring of blood glucose (SMBG) and continuous glucose monitoring (CGM) data;
- Safety of PaQ by local site effects, adverse events, hypoglycemic episodes (≤70 mg/dL) (9), and hyperglycemia associated with the use of PaQ;
- Patient satisfaction with PaQ using a questionnaire developed by the sponsor.

Main inclusion criteria were: T2D; age 30–65 years; HbA_{1c} ≤9.0% (75 mmol/mol) with stable MDI regimens. Main exclusion criteria were: insulin requirements >100 U/day, basal insulin alone or premixed insulin; current sulphonylurea therapy. The study was approved by the local ethics committee and performed in accordance with the Declaration of Helsinki and the principles of Good Clinical Practice at Medical University of Graz. All participants provided written informed consent prior to study participation.

Baseline

Participants used a blood glucose meter (One Touch Ultra; LifeScan, Inc., Milpitas, CA) to perform SMBG. Participants were asked to perform daily four-point profiles (premeal and bedtime) and seven-point profiles twice weekly (additional measurements 1.5 h after meals). Participants used a diary throughout the study to record SMBG values, hypoglycemia, insulin doses, and carbohydrate intake. Blinded CGM

(Dexcom Seven STS; Dexcom, San Diego, CA) was performed throughout the study.

Transition to PaQ

Participants received 1 h of training using the device and the PaQ Quick Start Guide as the primary teaching tool. Participants demonstrated their ability to assemble, apply, and safely use PaQ under supervision of the investigator. Participants were started on one of the five available preset PaQ basal doses using insulin aspart (Novo Nordisk A/S, Baegsvard, Denmark). The first selected basal dose was equal to or less than the basal dose used during baseline. Investigators adjusted basal doses if 20–25% gains/reductions in fasting blood glucose were seen relative to baseline. There was no optimization of the insulin dose in order to achieve glycemic targets. Meal bolus doses were dependent on carbohydrate intake. The first 24 h on PaQ were spent at the clinical research unit under supervision of the investigators, and thereafter, participants were seen every 3 days. Seven-point glucose profiles were performed daily.

PaQ Treatment

Participants managed their blood glucose independently by using PaQ following the same regimen used during baseline and documenting their test results and therapy as described earlier. Patient satisfaction and acceptance was assessed at the end of the study.

Data are presented as mean ± SD if not otherwise specified. Paired *t* tests were used to determine statistical significance ($P < 0.05$). Categorical, qualitative variable summaries included the frequency and percentage of participants who were in the particular category. The denominator for the percentage calculation was based upon the total number of participants in the intent-to-treat population (i.e., all participants who received PaQ at least once).

RESULTS

Twenty individuals with T2D (5 females) were enrolled in the study. Baseline characteristics included: HbA_{1c} 7.7 ± 0.7% (60 ± 7 mmol/mol), age of 59 ± 5 years, weight of 96.1 ± 13.7 kg, BMI of 32.1 ± 5.6 kg/m^2, and diabetes duration of 15 ± 7 years. Nineteen participants successfully transitioned from MDI to PaQ; 1 participant violated the protocol by discontinuing basal insulin application during baseline and was excluded. Another participant withdrew informed consent after the transition period because of no improvement in glycemic control.

Nineteen of 19 participants were able to assemble, fill, prime, bolus dose, and change the PaQ device as well as correctly interpret the communication signals emitted by PaQ and respond adequately.

Transition was successful in 14 of 19 participants using the first basal dose, and 5 required another dose change. TDD at baseline (60.4 ± 19.1 U) was similar to PaQ treatment (57.1 ± 14.6 U). A total of 50% of participants reduced their TDD by 26% (8–23 U) at study end. TDD for five patients remained unchanged (TDD within 10% of baseline dose), whereas TDD for four patients increased by ≥10% during PaQ treatment. The average number of daily bolus doses showed a slight increase during PaQ treatment (3.7 vs. 4.2; $P = 0.095$).

Changes in SMBG during PaQ treatment showed a trend toward improved glycemic control (pre- and postbreakfast and bedtime, all not significant) (Fig. 1*C*). CGM data revealed a reduction in average 24-h glucose exposure of −190.3 mg/dL ($P = 0.18$) compared with baseline. The reduction overnight was −101.7 mg/dL ($P = 0.06$). Time within target (70–140 mg/dL) increased from 30.7 to 35.6% ($P = 0.26$). The percentage of time that glucose values were <50 and <70 mg/dL showed a slight, but nonsignificant, increase during PaQ treatment.

Patient-reported data from the device-use questionnaire revealed a high level of PaQ satisfaction and acceptance. All but one scored >4.00, indicating high and very high device satisfaction, and the mean "acceptance" score ranked between high and very high.

No serious adverse events occurred during the study. Fourteen of 19 participants (73.7%) experienced hypoglycemic episodes, but none of these were associated with PaQ malfunction. The number of participants who experienced hypoglycemia was lower during PaQ treatment compared with baseline (Fig. 1*D*). A total of six device-associated hyperglycemic episodes (nonfunctional bolus button [*n* = 1], cannula dislodgment from skin [*n* = 2], device falling-off body [*n* = 1]) were experienced by 4 of 19 participants (21%). For two episodes in one participant, the causes remain unclear.

CONCLUSIONS

Data from this feasibility study suggest that PaQ is an easy-to-use, safe, and highly accepted continuous subcutaneous insulin infusion device. These findings are important because ease of use and improved patient satisfaction may result in better adherence and improved clinical outcomes (10). While the study is limited due to its size and lack of control group, the data suggest that PaQ may achieve glycemic control comparable to MDI. Additional studies are needed to elucidate the benefits of PaQ treatment in diverse diabetes populations.

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Author Contributions. J.K.M. and L.C.L. designed and performed the study, interpreted data, and drafted the manuscript. F.A. and S.K. performed the study, interpreted data, contributed to discussions, and critically revised the manuscript. E.S. and R.S.M. determined the methodology for the collection, analysis, and interpretation of the continuous glucose-monitoring data, contributed to discussions, and critically revised the manuscript. P.D. designed the study, interpreted data, contributed to discussions, and critically revised the manuscript. T.R.P. designed the study, supervised the project, contributed to discussions, and critically revised the article. All authors approved the final version of the manuscript. T.R.P. is the guarantor of this work and, as such, had full access to all the data in the

study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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