Feasibility of Outpatient 24-Hour Closed-Loop Insulin Delivery

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Studies using outpatient closed-loop insulin delivery for type 1 diabetes have recently been published (1–5). We conducted a 5-day outpatient feasibility study comparing hybrid closed-loop (HCL) to sensor-augmented pump therapy with low-glucose suspend (SAPT + LGS) in eight patients with type 1 diabetes using an open-label randomized crossover trial design (ACTRN12614001005640). We used the Medtronic HCL system: MiniMed insulin pump, MiniMed Enlite II glucose sensor, MiniMed MiniLink REAL-time sensor, MiniMed Translator, and an Android mobile device with the algorithm (proportional integrative derivate with insulin feedback and additional safety parameters—primarily being an upper limit of allowable insulin delivery). Multiple algorithm parameters were individualized according to total daily insulin requirements in the preceding 48 h. Meals were announced by entering a capillary glucose value and meal carbohydrate content, for which bolus insulin was delivered according to the patient's unique carbohydrate ratio. The Android mobile device sent data via the Internet, allowing for remote monitoring. During SAPT + LGS, the LGS threshold was set at 3.3 mmol/L. Sensor alarms were set at 3.9–18 mmol/L in both arms. Hyperglycemia was corrected according to the patient's sensitivity factor during SAPT +LGS and HCL. The outpatient phase was preceded by a 48-h in-clinic training phase in both arms. Participants checked capillary blood glucose 6–8 times per day, including an overnight check. Participants were contacted by phone twice a day and electronically monitored remotely 24 h a day. A continuous glucose monitor change was scheduled during both study arms.

Eight subjects (four adults aged 30–40 years and four adolescents aged 13–18 years, mean HbA_{1c} 7.5 ± 0.6% [58 ± 5 mmol/mol]) were studied. Results are shown in Table 1. There was no difference in the median total time spent in target (4.0–9.9 mmol/L) glucose sensor range: 67.6% for HCL versus 58.7% for SAPT + LGS ($P = 0.30$). Median sensor glucose was 8.2 mmol/L (6.6, 10.6) for HCL versus 8.9 mmol/L (6.7, 11.3) for SAPT + LGS ($P = 0.47$). At night, time spent in target sensor glucose range was similar for HCL (68.9%) and SAPT + LGS (67.8%) ($P = 0.76$). During the day, time spent in target sensor glucose range was 66.7% for HCL versus 57.5% for SAPT + LGS ($P = 0.18$). During HCL, there were seven hypoglycemic events (capillary blood glucose <3.3 mmol/L). Of these, three events occurred within 2 h of a bolus and three events occurred during exercise. During the SAPT + LGS phase, there were 13 hypoglycemic events (<3.3 mmol/L): 6 events occurred within 2 h of a bolus and 1 event occurred during exercise. The insulin pump automatically suspended in 10 of these events, and in one case the pump had been manually suspended. Hypoglycemia <2.8 mmol/L was all but eliminated with HCL (1 vs. 9, $P = 0.04$) (one event occurring after an open-loop correction bolus for hyperglycemia secondary to insulin infusion site failure). No occasions of investigator intervention were indicated. There were no adverse events.

This study used a prototype algorithm and demonstrated feasibility for home use. In response to the data, the algorithm has been improved to be more adaptive and incorporated into insulin pump hardware (MiniMed 670G) in preparation for long-term home studies.

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Table 1—Glucose control during HCL and SAPT + LGS over the 5-day phase in eight subjects with type 1 diabetes

	HCL	SAPT + LGS	*P**
Percent time spent at glucose level (mmol/L)			
<3.3	0.5 (0.0, 0.9); 0.54 ± 0.6	0.6 (0.0, 1.6); 1.13 ± 1.5	0.84
3.3–3.9	1.0 (0.4, 1.5); 1.15 ± 1.0	1.4 (0.2, 3.8); 1.98 ± 2.0	0.89
4.0–9.9	67.6 (61.4, 71.5); 67.41 ± 9.8	58.7 (52.7, 73.9); 60.97 ± 16.4	0.30
10.0–14.9	27.5 (22.0, 32.1); 26.44 ± 9.1	30.9 (22.2, 38.8); 30.17 ± 12.9	0.50
≥15	4.5 (2.9, 6.1); 4.46 ± 3.1	5.0 (0.7, 6.9); 5.75 ± 6.2	0.34
Sensor glucose (mmol/L)	8.2 (6.6, 10.6); 8.8 ± 3.1	8.9 (6.7, 11.3); 9.2 ± 3.4	0.47
Duration of observation (h)	929	926	N/A
Hypoglycemic events			
<3.9 mmol/L	18	26	0.23§
<3.3 mmol/L	7	13	0.19§
<2.8 mmol/L	1	9	0.04§

Data shown as median (interquartile range); mean ± SD or *n*. **P* value from a generalized estimate equation of daily data adjusted for the within-person clustering; for 4–9.9 and 10–14.9 mmol/L, percent time in range per day was used; for <3.3, 3.3–3.9, and ≥15 mmol/L, a dichotomous variable per day was analyzed under the binomial distribution. §*P* value calculated via Poisson regression, with duration of observation as the offset variable.

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