SUPPLEMENTARY DATA

SUPPLEMENTAL APPENDIX

RESEARCH DESIGN AND METHODS

Study procedures - inpatient study

Participants were admitted for one 22 h period in hospital for OCL control. The protocol was approved by Stanford University institutional review board. Written informed consent was obtained prior to the inpatient admission. Participants were eligible to participate if they were between 10-18 y of age, diagnosed with type 1 diabetes for at least 12 months and using an insulin pump for at least 3 months. Exclusion criteria included diabetes ketoacidosis in the preceding 30 days, hypoglycemic seizure or loss of consciousness in the preceding 3 months, pregnancy, history of a seizure disorder, cystic fibrosis, and other medical or psychiatric conditions considered to interfere with completion of the protocol. There was no A1C exclusion criteria.

The inpatient phase was designed to mimic the first day of camp. For each study night, four participants arrived at 1000 h on the day of the admission. One Dexcom Gen 4 Platinum glucose sensor was inserted per patient and calibrated before lunch. All calibrations were performed using fingerstick meter blood glucose values measured by the Bayer Contour Next USB glucometer (Bayer HealthCare, Leverkusen, Germany). The first calibration was entered approximately 2 h after sensor insertion, prior to lunch. Additional calibrations were entered prior to dinner and the bedtime snack.

Participants engaged in two periods of exercise, in the afternoon and after dinner, with the aim of achieving an elevated heart rate of between 100-140 bpm for 30 minutes. The activities ranged from group activities such as soccer and football to individual treadmill running and bike riding.

An intravenous cannula was inserted at 2000 h to allow for overnight venous blood sampling every 30 minutes for the duration of closed-loop control. Plasma glucose values were measured using YSI 2300 Stat Plus Glucose Analyzer (Yellow Springs Instrument, Life Sciences, Yellow Springs, OH). Overnight closed-loop was commenced between 2100 to 2200 h after a bedtime snack at approximately 2000 h. At the start of closed-loop, the Tandem tslim® insulin pump replaced the patient's own pump and a steel infusion set (Contact^{TM} Detach, Unomedical AS, Denmark) was inserted. Closed-loop control was stopped before breakfast between 0700 to 0730 h the next morning. Patients were discharged after breakfast.

Sensor calibration during closed-loop

In addition to the venous samples collected every 30 minutes, fingerstick meter glucose values were obtained at 0000, 0300 and 0600 h. If the sensor glucose differed from the meter glucose by more than 20%, the meter glucose was entered as a calibration value and a repeat meter glucose reading was obtained one hour later. If the second reading differed from the sensor glucose by > 20%, closed-loop was stopped.

Safety parameters

Closed-loop control was initiated if sensor glucose values were between 80 - 250 mg/dL and sensor error was ≤ 20%. If during closed-loop control, a sensor glucose value was < 70 mg/dL, a meter glucose value was obtained. If the meter glucose value was also < 70 mg/dL, the patient received carbohydrate treatment. A repeat blood glucose value was obtained after 15 minutes to ensure glucose levels were > 70 mg/dL post treatment. Closed-loop control continued in this instance.

If sensor glucose values were > 250 mg/dL, a meter glucose value was obtained and if verified, blood ketone levels were obtained. If blood ketone levels were ≤ 0.6 mmol/L, closed-loop control continued. If ketone levels were > 0.6, closed-loop control was stopped, and patients received a subcutaneous insulin correction dose, a new insulin infusion set was inserted and closed-loop control was suspended for 2 h.

Closed-loop was suspended for the individual patient if meter or plasma glucose values were <50 mg/dL or >400 mg/dL.

RESULTS

SUPPLEMENTARY DATA

Inpatient study

Closed-loop was started in 11 of 12 nights (92%) and did not start in one patient due to sensor failure.
Closed-loop proceeded uninterrupted in 9 nights (82%). In one patient, the algorithm stopped functioning and was delivering basal insulin only. The system was restarted and closed-loop continued for the remainder of the night. We were not able to reproduce this problem in simulation. In a second case, the pump and the controller phone became unpaired for 30 minutes. The system was restarted and closed-loop was resumed.

Intention to treat

Infusion set failure

There were four episodes of infusion set failure. On two occasions, glucose values were noted to be rising in the presence of ketonemia within hours of infusion set insertion. On a third occasion, the infusion set was found disconnected from the patient even though it was connected to the patient at the beginning of the night. On the fourth occasion, there was insulin non-delivery despite the insertion of one steel cannula and replacement of a second cannula within hours in the same patient. We suspected pump failure in this instance but could not be certain whether this was due to the pump mechanics, insulin cartridge irregularities or infusion set failure. The pump was returned to Tandem Diabetes for diagnostics but they were unable to find or reproduce any malfunction attributed to the pump or cartridge. At that time, given the information we had, we considered the cause of failure to be due to infusion set failure.