WITHDRAWAL OF REMOTE REAL-TIME TELEMETRIC MONITORING INCREASES HYPOGLYCEMIA DURING USUAL CARE BUT NOT DURING AUTOMATED GLUCOSE MANAGEMENT WITH AN INSULIN-ONLY OR BIHORMONAL BIONIC PANCREAS

Courtney Balliro, R.N.[1], Rabab Z. Jafri, M.D.[1], Michele Maheno, R.N.[1], Mallory A. Hillard, R.N.[1], Alexander O'Donovan, B.S.[2], Rajendranath R. Selagamsetty, B.S.[2], Firas H. El-Khatib, Ph.D.[2], Edward R. Damiano, Ph.D.[2], Steven J. Russell, M.D. Ph.D.[1]

[1] Diabetes Research Unit, Massachusetts General Hospital, Boston, MA
[2]Department of Biomedical Engineering, Boston University, Boston, MA

ABSTRACT

In previous adult outpatient studies of the bionic pancreas (BP), remote telemetric monitoring for hypoglycemia (monitoring) was performed in all arms, including the usual care (UC) arms. When continuous glucose monitoring glucose (CGMG) remained <50 mg/dl for ≥15 minutes study staff would contact the participant. This study aimed to evaluate the safety of eliminating monitoring from the BP and UC arms. We compared the BP with the lowest glucose targets that we have tested (bihormonal at 100 mg/dl [BH100] and insulin-only at 110 mg/dl [IO110]) with UC (insulin pump therapy or sensor-augmented pump therapy), each with and without monitoring for 7 days, in a random-order, six-week, crossover study, in 23 adult subjects with T1DM. The primary outcome was percentage of time spent hypoglycemic (CGMG <60 mg/dl). There was more hypoglycemia without monitoring vs. with monitoring in the two UC arms (1.2 vs. 0.9%, p=0.03). However, there was no difference in hypoglycemia without monitoring vs. with monitoring in the two BH100 (0.8 vs. 0.9%, p=0.90) and two IO110 (1.2 vs. 1.3%, p=0.77) arms. There were no pairwise mean CGMG differences between the two BH100, two IO110, and two UC arms. Without monitoring, hypoglycemia was reduced in BH100 vs. UC (0.9 vs. 1.2%, p=0.02) and was comparable in IO110 vs. UC (1.2 vs. 1.2%, p=0.47). The mean CGMG was significantly lower in all BP vs. UC arms.

METHODS

- The study consisted of six 7-day arms: two UC, two BH100, and two IO110. Each arm was completed twice in random order: once with 24 hour remote monitoring for severe biochemical hypoglycemia (CGMG < 50 mg/dl), and once without.
- All study arms included remote monitoring for device connectivity
- Volunteers went about their usual routines at home, work, etc. with no limitations on diet or exercise
- Primary outcome: Mean % time CGMG < 60 mg/dl (days 2-7)
- Key Secondary outcomes:
- Mean CGMG (days 2-7)
- Time CGMG spent in clinically relevant ranges (days 2-7) including < 50 mg/dl, < 54 mg/dl, 70-180 mg/dl, and > 250 mg/dl
- We used the paired-sample t-test to compare study groups for outcomes with normally distributed data, and the Wilcoxon signed rank test for non-normally distributed data. For normally distributed outcomes, we have reported means and SDs, and for non-normally distributed outcomes we have reported medians and ranges.

RESULTS

Table 1: Baseline Characteristics

Number of patients (% female)	23 (74%)
Age (years)	38 ± 13.6 (22.7-79.2)
Weight (kg)	80.2 ± 16.5 (54.9-127.7)
BMI (kg/m2)	28.4 ± 6.0 (21.9-48.7)
Diabetes Duration (years)	24.6 ± 8.9 (11-46)
Total Daily Insulin Dose (u/kg)	0.56 ± 0.15 (0.29-0.9)
Hemoglobin A1c (%)	7.2 ± 1.0 (5.3-9.1)

RESULTS

Removal of remote monitoring was associated with significantly more hypoglycemia (% < 60) under UC (p=0.03), but had no effect on hypoglycemia while using the BH100 (p=0.90) or IO110 (p=0.77). Total carb intake was significantly decreased only in the monitored UC arm (p=0.03) and removal of remote monitoring had no effect on time in range or TDD during UC, IO110, or BH100.

When comparing only unmonitored arms BH100 was statistically superior to both IO110 and UC for mean CGM glucose (p=0.00001, p<0.00001) and % time <60 mg/dl. (p=0.02, p=0.02). IO100 was statistically superior to UC for mean CGM glucose (p=0.004) but not for % time <60 mg/dl (p=0.47).

When comparing only unmonitored arms BH100 was statistically superior to both UC and IO110, and IO110 was statistically superior to UC, for time in range (70-180 mg/dl).

Table 2: Difference Between Monitored and Unmonitored Usual Care (UC), Insulin-Only (IO) and Bi-hormonal (BH) Arms

CGM Glucose Data	UC Not Monitored	UC Monitored	p value (Not Mon. vs. Mon)	IO Bionic Pancreas Not Monitored	IO Bionic Pancreas Monitored	p value (Not Mon. vs. Mon)	BH Bionic Pancreas Not Monitored	BH Bionic Pancreas Monitored	p value (Not Mon. vs. Mon)
Overall Mean (mg/dL)	164.8 (29.0)	164.1 (29.1)	0.83	148.5 (11.2)	151.1 (13.3)	0.14	138.5 (10.9)	138.6 (13.0)	0.97
<54 (% of time)	0.6 (0-6.1)	0.35 (0-3.7)	0.03	0.64 (0-3.3)	0.5 (0-2.3)	0.78	0.2 (0-2.1)	0.2 (0-3.2)	0.51
<60 (% of time)	1.2 (0-7.2)	0.9 (0-5.2)	0.03	1.2 (0-5.2)	1.3 (0-3.9)	0.77	0.8 (0-3.2)	0.9 (0-4.17)	0.90
70-180 (% of time)	59.5 (16.7)	60.6 (16.1)	0.66	72 (9.9)	70.8 (8.1)	0.39	78.6 (8.5)	78.7 (8.0)	0.93
>250 (% of time)	9.6 (0-35.6)	8.48 (0-43.0)	0.72	4.34 (0.5-12.4)	4.7 (1.0-16.5)	0.04	3.1 (0-10.0)	4.2 (0-11.6)	0.39
Total carbs (grams)	20.2	13.2	0.03	19.2	23.6	0.16	11.9	11.8	0.97
TDD insulin (u/kg/day)	0.54	0.52	0.15	0.59	0.61	0.44	0.64	0.62	0.5

CONCLUSIONS

Removal of remote monitoring for hypoglycemia had no effect on hypoglycemia or any other performance parameter of the insulin-only and bihormonal configurations of the bionic pancreas. The bihormonal bionic pancreas was superior to the insulin-only bionic pancreas for hypoglycemia and mean CGM glucose. The insulin-only bionic pancreas was superior to usual care for mean CGM glucose and was nominally better for hypoglycemia, although this difference was not statistically significant. Monitoring for hypoglycemia can be safely removed in future studies of both the bihormonal and insulin-only bionic pancreas.

REFERENCES/DISCLOSURES

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- AO, RRS, FEK, and ERD are employees of Beta Bionics, and RRS, FEK, and ERD have equity in Beta Bionics. FEK, ERD and SJR have patents and patents pending on the bionic pancreas.

Figure 1: Average CGMG and % <60 mg/dl for each bionic pancreas configuration and usual care. Each line represents a single subject.