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ORIGINAL ARTICLE

Decision Support Systems and Closed Loop

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Introduction

THIS YEAR WAS NOTABLE FOR GREAT advances in the implementation of closed-loop systems for clinical use. The Medtronic Minimed 670G hybrid closed-loop (HCL) system is now in regular use in clinical practice in the United States. The Tandem predictive low-glucose suspend (PLGS) system, branded as Basal-IQ, uses the Tandem X2 insulin pump and the Dexcom G6 continuous glucose monitor (CGM). This system was approved by the U.S. Food and Drug Administration and then released to consumers in August 2018 after showing a 31% reduction in percent time below 70 mg/dL compared with sensor-augmented pump (SAP) therapy in a randomized crossover outpatient trial (1). Clinical trial results of using the Omnipod personalized model predictive control algorithm, planned for eventual use in the Insulet OmniPod® Horizon automated glucose control system, a single-hormone HCL system, have also been published (2,3). Multiple other commercial and academic long-term trials of closed-loop systems are under way, including four U.S. National Institutes of Health–awarded multicenter studies with sites from Europe and the United States (FlorenceM system/Cambridge, UK; inControl/Virginia, United States; iLet system/Boston, United States; and Flair/Medtronic & MD-Logic system) designed to be the potential last steps for regulatory approval of these systems. All aim to demonstrate clinical effectiveness to facilitate regulatory approval and future reimbursement of these devices (4). Closed-loop systems have now been tested in various settings, for hospitalized patients as well as throughout pregnancy to include delivery and the postpartum period (5,6).

Additionally, this year's article adds a section on decision support systems. These tools can support treatment decisions for a wide range of patients, whether they are treated with injections or pump and monitor glucose with glucometer or CGM or any other modality, as some patients will not be able or want to use a closed-loop system. The systems include smart pens with automated titration and dosing adjustment recommendations, analysis tools built into web-based or app software that can make dosing recommendations for patients on multiple daily injections or using insulin pumps, or mobile software with glucose prediction capabilities. By providing automated tools to optimize clinical outcomes, decision support systems have the potential to improve clinical outcomes and may increase access to care as they become accessible to more patients, enhancing utilization of health-care resources by integrating e-health and telemonitoring programs. It should not be surprising that some closed-loop systems have integrated automated decision support systems, adjusting baseline basal rates based on feedback from the use of closed-loop control or by adding automated input from additional sensors such as heart rate and activity monitoring into their algorithms, and are listed as such below.

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Key Articles Reviewed for the Article

Adjusting insulin doses in patients with type 1 diabetes that use insulin pump and continuous glucose monitoring: variations among countries and physicians

Nimri R, Dassau E, Segall T, Muller I, Bratina N, Kordonouri O, Bello R, Biester T, Dovc K, Tenenbaum A, Brener A, Šimunović M, Sakka SD, Nevo Shenker M, Passone CG, Rutigliano I, Tinti D, Bonura C, Caiulo S, Ruszala A, Piccini B, Giri D, Stein R, Rabbone I, Bruzzi P, Omladič JŠ, Steele C, Beccuti G, Yackobovitch-Gavan M, Battelino T, Danne T, Atlas E, Phillip M

*Diabetes Obes Metab 2018; **20**: 2458–2466*

Continuous glucose monitoring and insulin informed advisory system with automated titration and dosing of insulin reduces glucose variability in type 1 diabetes mellitus

Breton MD, Patek SD, Lv D, Schertz E, Robic J, Pinnata J, Kollar L, Barnett C, Wakeman C, Oliveri M, Fabris C, Chernavvsky D, Kovatchev BP, Anderson SM

*Diabetes Technol Ther 2018; **20**: 531–540*

Decision support in diabetes care: the challenge of supporting patients in their daily living using a mobile glucose predictor

Pérez-Gandía C, García-Sáez G, Subías D, Rodríguez-Herrero A, Gómez EJ, Rigla M, Hernando ME

*J Diabetes Sci Technol 2018; **12**: 243–250*

Twelve-week 24/7 ambulatory artificial pancreas with weekly adaptation of insulin delivery settings: effect on hemoglobin A1c and hypoglycemia

Dassau E, Pinsker JE, Kudva YC, Brown SA, Gondhalekar R, Dalla Man C, Patek S, Schiavon M, Dadlani V, Dasanayake I, Church MM, Carter RE, Bevier WC, Huyett LM, Hughes J, Anderson S, Lv D, Schertz E, Emory E, McCrady-Spitzer SK, Jean T, Bradley PK, Hinshaw L, Laguna Sanz AJ, Basu A, Kovatchev B, Cobelli C, Doyle III, FJ

*Diabetes Care 2017; **40**: 1719–1726*

Randomized outpatient trial of single- and dual-hormone closed-loop systems that adapt to exercise using wearable sensors

Castle JR, El Youssef J, Wilson LM, Reddy R, Resalat N, Branigan D, Ramsey K, Leitschuh J, Rajhbeharrysingh U, Senf B, Sugerman SM, Gabo V, Jacobs PG

*Diabetes Care 2018; **41**: 1471–1477*

Closed-loop insulin delivery for glycemic control in noncritical care

Bally L, Thabit H, Hartnell S, Andereggen E, Ruan Y, Wilinska ME, Evans ML, Wertli MM, Coll AP, Stettler C, Hovorka R

*N Engl J Med 2018; **379**: 547–556*

Overnight glucose control with dual- and single-hormone artificial pancreas in type 1 diabetes with hypoglycemia unawareness: a randomized controlled trial

Abitbol A, Rabasa-Lhoret R, Messier V, Legault L, Smaoui M, Cohen N, Haidar A

*Diabetes Technol Ther 2018; **20**: 189–196*

Closed-loop control during intense prolonged outdoor exercise in adolescents with type 1 diabetes: the artificial pancreas ski study

Breton MD, Cherñavvsky DR, Forlenza GP, DeBoer MD, Robic J, Wadwa RP, Messer LH, Kovatchev BP, Maahs DM

*Diabetes Care 2017; **40**: 1644–1650*

Overnight closed-loop control improves glycemic control in a multicenter study of adults with type 1 diabetes

Brown SA, Breton MD, Anderson SM, Kollar L, Keith-Hynes P, Levy CJ, Lam DW, Levister C, Baysal N, Kudva YC, Basu A, Dadlani V, Hinshaw L, McCrady-Spitzer S, Bruttomesso D, Visentin R, Galasso S, Del Favero S, Leal Y, Boscari F, Avogaro A, Cobelli C, Kovatchev BP

*J Clin Endocrinol Metab 2017; **102**: 3674–3682*

Closed-loop glucose control in young people with type 1 diabetes during and after unannounced physical activity: a randomised controlled crossover trial

Dovc K, Macedoni M, Bratina N, Lepej D, Nimri R, Atlas E, Muller I, Kordonouri O, Biester T, Danne T, Phillip M, Battelino T

*Diabetologia 2017; **60**: 2157–2167*

Fully closed-loop multiple model probabilistic predictive controller artificial pancreas performance in adolescents and adults in a supervised hotel setting

Forlenza GP, Cameron FM, Ly TT, Lam D, Howsmon DP, Baysal N, Kulina G, Messer L, Clinton P, Levister C, Patek SD, Levy CJ, Wadwa RP, Maahs DM, Bequette BW, Buckingham BA

*Diabetes Technol Ther 2018; **20**: 335–343*

Impact of macronutrient content of meals on postprandial glucose control in the context of closed-loop insulin delivery: a randomized cross-over study

Gingras V, Bonato L, Messier V, Roy-Fleming A, Smaoui MR, Ladouceur M, Rabasa-Lhoret R

*Diabetes Obes Metab 2018; **20**: 2695–2699*

Evaluation of an artificial pancreas with enhanced model predictive control and a glucose prediction trust index with unannounced exercise

Pinsker JE, Laguna Sanz AJ, Lee JB, Church MM, Andre C, Lindsey LE, Doyle III, FJ, Dassau E

*Diabetes Technol Ther 2018; **20**: 455–464*

Ketone production in children with type 1 diabetes, ages 4–14 years, with and without nocturnal insulin pump suspension

Wadwa RP, Chase HP, Raghinaru D, Buckingham BA, Hramiak I, Maahs DM, Messer L, Ly T, Aye T, Clinton P, Kollman C, Beck RW, Lum J; for the In Home Closed Loop Study Group

*Pediatr Diabetes 2017; **18**: 422–427*

Predictive hyperglycemia and hypoglycemia minimization: in-home double-blind randomized controlled evaluation in children and young adolescents

Forlenza GP, Raghinaru D, Cameron F, Bequette BW, Chase HP, Wadwa RP, Maahs DM, Jost E, Ly TT, Wilson DM, Norlander L, Ekhlaspour L, Min H, Clinton P, Njeru N, Lum JW, Kollman C, Beck RW, Buckingham BA; for the In-Home Closed-Loop (IHCL) Study Group

*Pediatr Diabetes 2018; **19**: 420–428*

CLINICAL DECISION SUPPORT SYSTEMS

Adjusting insulin doses in patients with type 1 diabetes that use insulin pump and continuous glucose monitoring: variations among countries and physicians

Nimri R[1], Dassau E[2], Segall T[3], Muller I[3], Bratina N[4], Kordonouri O[5], Bello R[1], Biester T[5], Dovc K[4], Tenenbaum A[1,6], Brener A[1], Šimunović M[7], Sakka SD[8], Nevo Shenker M[1], Passone CG[9], Rutigliano I[10], Tinti D[11], Bonura C[12], Caiulo S[12], Ruszala A[13], Piccini B[14], Giri D[15], Stein R[16], Rabbone I[11], Bruzzi P[17], Omladič JŠ[4], Steele C[18], Beccuti G[19], Yackobovitch-Gavan M[1], Battelino T[4,20], Danne T[5], Atlas E[3], Phillip M[1,6]

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*Diabetes Obes Metab 2018; **20**: 2458–2466*

Background

There can be considerable variability among physicians when making recommendations for adjusting insulin pump settings based on clinical analysis of CGM, insulin pump, and glucometer data for patients with type 1 diabetes. Automated insulin adjustments based on computerized analysis of these data offer the potential of greater access to care and reduced variability in recommended dose changes.

Methods

Twenty-six physicians from 16 centers across Europe, Israel, and South America were asked to adjust insulin dosing based on device download data from 15 patients (mean age 16.2 ± 4.3 years, 6 female, mean glycated hemoglobin [HbA1c] 8.3 ± 0.9%) gathered over a 3-week period. These recommendation adjustments were compared for relative changes in the basal rates, carbohydrate/insulin ratio (CR), and correction factor (CF) among physicians and among centers, as well as between doctors and DreaMed Advisor Pro, an automated algorithm. Results were calculated from the percentage of comparison points for which all methods agreed on the trend of insulin dose adjustments (same trend) and those for which there was partial agreement (increase/decrease vs no change) and full disagreement (opposite trends).

Results

Full agreement between physicians on the trend of insulin adjustments occurred at a rate of 41 ± 9% for basal, 45 ± 11% for CR, and 45.5 ± 13% for CF plans. Complete disagreement percentages were 12 ± 7%, 9.5 ± 7%, and 10 ± 8%, respectively. Similar results were found when comparing the physicians and Advisor Pro. The magnitude of the Advisor insulin dose changes was never greater than those proposed by physicians.

Conclusions

The automated advice of the DreaMed Advisor Pro did not differ significantly from the advice given by the physicians in the direction or magnitude of the insulin dosing.

Comments

Automated analysis of diabetes device data (insulin pump, CGM, and glucometer) holds the promise of vastly increasing access to quality medical care for patients with diabetes. In this trial, the DreaMed Advisor Pro analyzed the same dataset as the physicians and came up with similar dose adjustment recommendations. Recently, the DreaMed Advisor Pro was approved by the U.S. Food and Drug Administration for integration with the popular Glooko software package, helping health-care providers make recommendations for changes in insulin pump therapy (7). This is the first step in moving toward increasing levels of automated dose advising, with the ultimate goal that patients can have the advisor software periodically analyze their device data, rather than waiting for clinician input to make adjustments, thus improving clinical care.

Continuous glucose monitoring and insulin informed advisory system with automated titration and dosing of insulin reduces glucose variability in type 1 diabetes mellitus

Breton MD, Patek SD, Lv D, Schertz E, Robic J, Pinnata J, Kollar L, Barnett C, Wakeman C, Oliveri M, Fabris C, Chernavvsky D, Kovatchev BP, Anderson SM

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*Diabetes Technol Ther 2018; **20**: 531–540*

Background

Glucose variability (GV) is a key limiting factor in successful diabetes management. Use of CGM and connected insulin delivery devices offers potential for expert systems to analyze this data and may further improve glucose outcomes and GV beyond use of these systems alone.

Methods

A total of 24 patients with type 1 diabetes (T1D) (15 women, 37 ± 11 years of age, HbA1c 7.2% ± 1%, total daily insulin 46.7 ± 22.3 U) using either an insulin pump or multiple daily injections with carbohydrate counting completed the study carried out over two randomized crossover 48-h visits at the University of Virginia. Each patient wore a Dexcom G4 CGM and used either usual care or the UVA decision support system

(DSS). DSS comprised a combination of automated insulin titration, bolus calculation, and carbohydrate treatment advice. Patients were exposed to meals of various size and contents in addition to two 45-min bouts of exercise. GV and glucose control outcomes were measured using CGM.

Results

The use of DSS significantly reduced GV (coefficient of variation 0.36 ± 0.08 vs 0.33 ± 0.06; $P = 0.045$) and maintained glycemic control (average CGM 155.2 ± 27.1 mg/dL vs 155.2 ± 23.2 mg/dL) by reducing exposure to hypoglycemia (< 70 mg/dL) (3.8% ±4.6% vs 1.8% ±2%; $P = 0.018$). DSS use also produced nonsignificant trends toward reduction of significant hyperglycemia (> 250 mg/dL) overnight (5.3% ± 9.5% vs 1.9% ±4.6%) and at mealtime (11.3% ± 14.8% vs 5.8% ±9.1%).

Conclusions

The device-informed advisory system was shown to be safe and feasible in a cohort of 24 subjects with T1D. Use of the system may reduce GV and improve protection against hypoglycemic events.

Comment

The decision support systems used in this study consisted of two real-time advisors (CGM-Informed Bolus Advisor and Exercise Advisor) and a retrospective insulin titration tool. The system was able to significantly reduce GV, likely through the reduction of exposure to hypoglycemia, without increasing average glycemia or exposure to hyperglycemia. Remarkably, it did this in a very short time (in a 48-hour crossover study). Thus, it appears that automated insulin titration, coupled with dosing and hypoglycemia real-time advice based on CGM, is safe, feasible, and may positively impact glucose control in T1D subjects using continuous subcutaneous insulin infusion or multiple daily injections.

Decision support in diabetes care: the challenge of supporting patients in their daily living using a mobile glucose predictor

Pérez-Gandía C[1,2], García-Sáez G[1,2], Subías D[3], Rodríguez-Herrero A[1,2], Gómez EJ[1,2], Rigla M[3], Hernando ME[1,2]

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*J Diabetes Sci Technol 2018; **12**: 243–250*

Background

Individuals with T1D actively manage their condition and need to have the knowledge to make decisions fitting their day-to-day insulin requirements. Artificial intelligence applications can aid decision making for patients and allow them to adjust more quickly than scheduled face-to-face visits. This work presents a DSS based on glucose prediction that assists patients via a mobile phone platform.

Methods

The system's impact on therapeutic corrective actions was evaluated through a randomized crossover pilot study focusing on between-meal periods. Twelve T1D subjects using insulin pumps participated in two phases. During the experimental phase participants used the DSS to alter initial corrective decisions in the presence of hypoglycemic or hyperglycemic events. During the control phase patients were directed to make corrective decisions without the DSS glucose prediction. A telemedicine interface allowed participants to record glucose monitoring data and decisions while endocrinologists also supervised data from the hospital. The study period was defined as a postprediction (PP) time window.

Results

When provided with the glucose prediction, patients modified their initial decision 20% of the time. No statistically significant differences were found in the PP Kovatchev's risk index change (ΔRI calculated for 1 h before the start and 1 h before the end of the postprandial time window): -1.23 ± 11.85 in experimental phase vs -0.56 ± 6.06 in control phase. In a usability questionnaire after the study, participants expressed positive opinions about the DSS, assigning it an average score higher than 7 (out of 9 total).

Conclusions

The DSS had a relevant impact in the participants' decision making while aiding T1D management and showed a high confidence of patients in the use of glucose prediction.

Comments

Although not achieving clinically significant improvements in glycemic results, this study highlights the importance of patient acceptance in clinical DSS recommendations. Based on the system recommendations, participants modified their initial decision 20% of the time. They also had a positive opinion about the DSS, with a high average score in a usability questionnaire despite having only limited use of the system. These usability issues and learning to have confidence in the system will be of paramount importance as more patients gain access to DSSs for home use.

CLOSED-LOOP SYSTEMS WITH AUTOMATED DECISION SUPPORT SYSTEMS

Twelve-week 24/7 ambulatory artificial pancreas with weekly adaptation of insulin delivery settings: effect on hemoglobin A1c and hypoglycemia

Dassau E[1,2], Pinsker JE[2], Kudva YC[3], Brown SA[4], Gondhalekar R[1,2], Dalla Man C[5], Patek S[4], Schiavon M[5], Dadlani V[3], Dasanayake I[2,6], Church MM[2], Carter RE[7], Bevier WC[2], Huyett LM[2,6], Hughes J[4], Anderson S[4], Lv D[4], Schertz E[4], Emory E[4], McCrady-Spitzer SK[3],

Jean T[2], Bradley PK[2], Hinshaw L[3], Laguna Sanz AJ[1,2], Basu A[3], Kovatchev B[4], Cobelli C[5], Doyle III, FJ[1,2]

[1]Harvard John A. Paulson School of Engineering and Applied Sciences, Harvard University, Cambridge, MA; [2]William Sansum Diabetes Center, Santa Barbara, CA; [3]Endocrine Research Unit, Mayo Clinic, Rochester, MN; [4]Center for Diabetes Technology, University of Virginia, Charlottesville, VA; [5]Department of Information Engineering, University of Padova, Padua, Italy; [6]Department of Chemical Engineering, University of California Santa Barbara, Santa Barbara, CA; [7]Department of Health Sciences Research, Mayo Clinic, Rochester, MN

*Diabetes Care 2017; **40**: 1719–1726*

Background

Because insulin analogs take time to reach peak serum concentration, adjustment of basal rate (either reduction/suspension or increase in insulin delivery) is not always enough to compensate for inaccuracies in meal bolus dosing, exercise, illnesses, stress, or other activities that change insulin sensitivity. The authors hypothesized that having patients on near optimal basal rates helps the artificial pancreas (AP) algorithms to be as effective as possible, as they work within a given constraint when reducing/suspending or giving extra insulin. To that end, they developed and tested a novel adaptive AP in an outpatient, single-arm, uncontrolled multicenter clinical trial lasting 12 weeks.

Methods

Thirty adults with T1D completed a 1-week sensor-augmented pump (SAP) run-in period. After the AP was started, basal insulin delivery settings used by the AP for initialization were adapted weekly, and carbohydrate ratios were adapted every 4 weeks by an algorithm running on a cloud-based server, with automatic data upload from devices. Adaptation recommendations were reviewed by expert study clinicians and participants before being implemented. The primary endpoint was change in HbA1c.

Results

Twenty-nine patients completed the trial. Mean HbA1c was 7.0 ± 0.8% at the start of AP use and decreased to 6.7 ± 0.6% after 12 weeks (−0.3 [95% CI −0.5 to −0.2]; $P < 0.001$). Compared with the SAP run-in, CGM time spent in the hypoglycemic range improved during the day from 5.0% to 1.9% (−3.1 [95% CI −4.1 to −2.1]; $P < 0.001$) and overnight from 4.1% to 1.1% (−3.1 [95% CI −4.2 to −1.9]; $P < 0.001$). Approximately 10% of adaptation recommendations were manually overridden by study physicians.

Conclusions

Use of the novel adaptive AP yielded significant reductions in HbA1c and hypoglycemia.

Comments

In this study, a cloud-based system seamlessly integrated data from AP use into an automated adaptation framework for basal rates and carbohydrate ratios throughout the 12-week period, potentially obviating the need for clinician involvement prior to or during use of AP to optimize open-loop settings. Percent time with glucose < 70 mg/dL significantly decreased during the day and overnight, while at the same time HbA1c decreased (−0.3% [95% CI −0.5 to −0.2]; $P < 0.001$). Although single arm and uncontrolled, this study showed automated adaptations of insulin pump settings can be performed safely and effectively to improve AP performance. Further studies are needed to best delineate how often these optimizations should occur and if they can be done in a completely automated manner without physician review in the future.

Randomized outpatient trial of single- and dual-hormone closed-loop systems that adapt to exercise using wearable sensors

Castle JR[1], El Youssef J[1,2], Wilson LM[1], Reddy R[2], Resalat N[2], Branigan D[1], Ramsey K[3], Leitschuh J[2], Rajhbeharrysingh U[1], Senf B[1], Sugerman SM[1], Gabo V[1], Jacobs PG[2]

[1]Harold Schnitzer Diabetes Health Center, Division of Endocrinology, Oregon Health and Science University, Portland, OR; [2]Department of Biomedical Engineering, Oregon Health and Science University, Portland, OR; [3]Oregon Clinical and Translational Research Institute Biostatistics and Design Program, Oregon Health and Science University, Portland, OR

*Diabetes Care 2018; **41**: 1471–1477*

This manuscript is also discussed in the article on Advances in Exercise, Physical Activity, and Diabetes Mellitus, page S-112.

Background

Exercise-related hypoglycemia remains a challenge, even with the use of AP systems. This study aimed to determine whether a dual-hormone closed-loop system with wearable sensors to detect exercise and adjust dosing to reduce exercise-related hypoglycemia would outperform other forms of closed-loop and open-loop therapy.

Methods

The study consisted of four arms—dual-hormone, single-hormone, PLGS, and continuation of current care—which participants completed in randomized order over 4 outpatient days. Each arm included three moderate-intensity aerobic exercise sessions. Physical activity and heart rate were captured with the ZephyrLife BioPatch and were incorporated into the AP algorithms during the study period. Primary outcomes were percent time in hypoglycemia (< 70 mg/dL) and percent time in target blood glucose range (70–180 mg/dL) assessed across the entire study and from the start of the in-clinic exercise until the next meal.

Results

Twenty adults with T1D completed all four arms. Mean time (SD) in hypoglycemia was lowest with dual-hormone

during the exercise period: 3.4% (4.5) vs 8.3% (12.6) with single-hormone ($P=0.009$) vs 7.6% (8.0) with PLGS ($P<0.001$) vs 4.3% (6.8) with current care, allowing pre-exercise insulin adjustments ($P=0.49$). Across the entire study, time in hypoglycemia was the lowest with dual-hormone treatment as well: 1.3% (1.0) vs 2.8% (1.7) for single-hormone treatment ($P < 0.001$) vs 2.0% (1.5) for PLGS ($P=0.04$) vs 3.1% (3.2) for current care ($P=0.007$). Time in range during the entire study was the highest with single-hormone vs dual-hormone treatment: 74.3% (8.0) vs 72.0% (10.8) ($P=0.44$).

Conclusions

In physically active adults with T1D, the addition of glucagon to a closed-loop system with automated exercise detection resulted in less time spent in hypoglycemia.

Comments

This study shows the potential of adding additional signals such as heart rate and activity monitoring into AP, comparing all modern modalities of insulin delivery systems, to include dual-hormone AP, single-hormone AP, PLGS, and SAP with dosing adjustments allowed prior to exercise. In a prior study without automated exercise detection, the authors showed that both dual-hormone AP as well as SAP with dosing adjustment allowed in advance of exercise could reduce the incidence of hypoglycemia equally as well (8). In this study, with the addition of automated exercise detection, the dual-hormone AP performed best, minimizing hypoglycemia both during exercise and during the entire 4-day period, highlighting how well AP can function with additional signals added as input into the AP algorithm. Future studies with more portable exercise monitors (such as wristwatches) that are conformable for patient wear will allow for long-term use of these devices in the outpatient setting.

CLOSED-LOOP SYSTEMS

Closed-loop insulin delivery for glycemic control in noncritical care

Bally L[1,2,3], Thabit H[3,6,7], Hartnell S[5], Andereggen E[1], Ruan Y[3], Wilinska ME[3,4], Evans ML[3,5], Wertli MM[2], Coll AP[3,5], Stettler C[1], Hovorka R[3,4]

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*N Engl J Med 2018; **379**: 547–556*

Background

For patients with diabetes, hospitalization can lead to poor glycemic control, adversely affecting outcomes. There already exists a significant evidence base for AP improving glycemic control in both the inpatient and outpatient settings in patients with T1D. This study investigated whether a closed-loop system could also improve glycemic control in hospitalized patients with type 2 diabetes (T2D) that were receiving noncritical care.

Methods

This randomized, open-label trial was conducted on general wards in two tertiary hospitals in the United Kingdom and Switzerland. A total of 136 adults with T2D who required subcutaneous insulin therapy were assigned to either the closed-loop insulin delivery group (70 patients) or conventional subcutaneous insulin therapy group (66 patients), according to local clinical practice. The primary endpoint was the percentage of time that the sensor glucose measurement was within the target range of 100–180 mg/dL (5.6–10.0 mmol/L) for up to 15 days or until hospital discharge.

Results

Mean (±SD) percent time in the target range was 65.8±16.8% in the closed-loop group and 41.5±16.9% in the control group, a difference of 24.3±2.9 percentage points ([95% CI 18.6–30.0]; $P<0.001$). Values above the target range were found in 23.6±16.6% and 49.5±22.8% of the patients, respectively, a difference of 25.9±3.4 percentage points ([95% CI 19.2–32.7]; $P<0.001$). Mean glucose level in the closed-loop group was 154 mg per deciliter (8.5 mmol/L) compared with 188 mg per deciliter (10.4 mmol/L) in the control group ($P<0.001$). Duration of hypoglycemia (glucose <54 mg/dL; $P=0.80$) was not significantly different between groups, nor was the amount of insulin delivered (median dose, 44.4 U and 40.2 U, respectively; $P=0.50$). There were no episodes of severe hypoglycemia or clinically significant hyperglycemia with ketonemia occurred in either trial group.

Conclusions

Among inpatients with T2D receiving noncritical care, the use of an automated, closed-loop insulin-delivery system resulted in significantly better glycemic control than conventional subcutaneous insulin therapy, without creating a higher risk of hypoglycemia.

Comment

This study builds upon prior work supporting that in this population, closed-loop insulin delivery without meal boluses can significantly improve glycemic outcomes in patient with T2D (9). This is in a diverse group of patients admitted for infection, kidney injury, cardiac disease, malignancy, and myriad other diagnoses. Given there are only a few studies on insulin pump use in people with T2D, this study shows the potential of AP in T2D treatment and the importance of advanced device use in this population, especially in the hospitalized patient.

Overnight glucose control with dual- and single-hormone artificial pancreas in type 1 diabetes with hypoglycemia unawareness: a randomized controlled trial

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Background

Dual-hormone (insulin and glucagon) AP may benefit certain populations more than others. This study sought to compare dual- and single-hormone AP systems in patients with hypoglycemia unawareness and documented nocturnal hypoglycemia.

Methods

This randomized crossover trial compared the effectiveness of dual- and single-hormone AP systems in controlling plasma glucose levels over the course of one night's sleep. Participants included 18 adult participants with hypoglycemia unawareness and 17 participants with hypoglycemia awareness, all of whom had documented nocturnal hypoglycemia during 2 weeks of screening. Outcomes were percent time with plasma glucose <4.0 mmol/L and number of hypoglycemic events (glucose <3.0 mmol/L).

Results

In participants with hypoglycemia unawareness, the median (interquartile range) percent time in hypoglycemia was 0% (0–0) on dual-hormone AP nights and 0% (0–10) on single-hormone AP nights ($P=0.20$), with two hypoglycemic events on dual-hormone AP nights and three hypoglycemic events on single-hormone AP nights. In contrast, in participants with hypoglycemia awareness, the median (interquartile range) percent time hypoglycemia was 0% (0–0) on both dual- and single-hormone AP nights, with zero hypoglycemic events on dual-hormone AP nights and one event on single-hormone AP nights. More glucagon was delivered to participants with hypoglycemia awareness compared with participants with hypoglycemia unawareness ($P=0.03$).

Conclusions

In this study, dual-hormone and single-hormone systems were equivalent in preventing nocturnal hypoglycemia in participants with hypoglycemia unawareness. Longer studies over the course of multiple days and nights may be needed to explore possible specific benefits in this population.

Comments

Dual-hormone AP, using both insulin and glucagon, has proven beneficial over single hormone (insulin only) AP in some prior studies, in particular in relation to exercise and hypoglycemia (10), while in other studies where was no difference (11). The challenge may be finding the right combination of situations (such as exercise or perhaps overnight only), select patient population (different age groups, hypoglycemia unawareness), and algorithms (with glucagon use fully integrated into the algorithm or just used as rescue dose for hypoglycemia) so that we can clearly denote these differences. The complexity and cost of dual-hormone delivery also remain barriers to be overcome and are tradeoffs compared with single-hormone systems, which can offer similar performance in some circumstances. Regardless, this study further builds on a growing body of literature showing both single- and dual-hormone AP were safe and effective and now supports AP use in the subpopulation of patients with hypoglycemia unawareness.

Closed-loop control during intense prolonged outdoor exercise in adolescents with type 1 diabetes: the artificial pancreas ski study

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This manuscript is also discussed in the article on Advances in Exercise, Physical Activity, and Diabetes Mellitus, page S-112, and the article on Diabetes Technology and Therapy in the Pediatric Age Group, page S-123.

Background

Extended vigorous outdoor exercise, common among adolescents, has not been well studied in the context of closed-loop control (CLC). Intense exercise is a major challenge to the management of T1D, yet most exercise studies to date of CLC show improved outcomes during shorter interval, limited-intensity activity.

Methods

Thirty-two adolescents with T1D (ages 10–16 years of age) participated in this randomized, controlled trial during a 5-day ski camp ($\sim$5 h skiing/day) at two sites (Wintergreen, VA, and Breckenridge, CO). Participants were randomly assigned to the University of Virginia CLC system or to a remotely monitored sensor-augmented pump (RM-SAP). The CLC and RM-SAP groups were generally paired by age and HbA1c. Study physicians and the clinical team remotely monitored all subjects 24 h per day.

Results

CLC increased the percentage of time in range (70–180 mg/dL) compared with physician-monitored open-loop therapy, to 71.3% vs 64.7% (+6.6% [95% CI 1–12]; $P = 0.005$), with maximum effect late at night. Hypoglycemia exposure and carbohydrate treatments both improved overall ($P = 0.001$ and $P = 0.007$) and during the daytime, with strong effects from skill level ($P = 0.0001$ and $P = 0.006$). Ski/snowboard proficiency level was balanced between groups but with a very strong site effect: naive in Virginia and experienced in Colorado. No adverse events were associated with the use of CLC, and feedback from the adolescent participants was overwhelmingly positive.

Conclusions

Even during intensive winter sport activities and their associated challenges, CLC in adolescents with T1D improved glycemic control and reduced exposure to hypoglycemia.

Comment

CLC has been well studied in shorter-duration exercise, but a major limitation of responding to real-time changes in CGM readings is a limited ability to prevent hypoglycemia. In fact, in a prior study, careful preparation by reducing basal insulin rates ahead of time performed just as well as dual-hormone CLC (8). Therefore, it was uncertain how a CLC system, in particular a single-hormone (insulin only) system, would respond to multiple hours of intense exercise each day, especially given the added challenges of cold and altitude. In this study, the University of Virginia CLC system showed improved outcomes over open-loop care, mainly by limiting hypoglycemia and reducing the need for carbohydrate treatment. As fear of hypoglycemia is a major barrier to performing exercise in this population (12), these encouraging results show the promise of CLC under very challenging conditions for people with T1D.

Overnight closed-loop control improves glycemic control in a multicenter study of adults with type 1 diabetes

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Background

The goal of this study was to analyze glycemic control in an overnight CLC system designed to ''reset'' the patient to near-normal glycemic targets every morning and to assess its effect on improved overall glycemic control overnight and during a 24-hour period, even though the system was active only overnight.

Methods

This was a randomized, crossover, multicenter clinical trial of 44 subjects with T1D requiring insulin pump therapy, comparing SAP at home vs 5 nights of CLC (active from 11:00 p.m. to 7:00 a.m.) in a supervised outpatient setting (research house or hotel), with a subsequent substudy of 5 nights of at-home CLC. Outcome was the percentage of time spent with glucose readings within the target range (70–180 mg/dL) measured using a CGM.

Results

Forty subjects (age 45.5 ± 9.5 years; HbA1c 7.4% ± 0.8%) completed the study. The use of CLC was associated with significant improvement in time in the target range (70–180 mg/dL) vs SAP, both over 24 hours (78.3% vs 71.4%; $P = 0.003$) and overnight (85.7% vs 67.6%; $P < 0.001$). The time spent in a hypoglycemic range also (< 70 mg/dL) decreased significantly in the CLC vs SAP group over 24 hours (2.5% vs 4.3%; $P = 0.002$) and overnight (0.9% vs 3.2%; $P < 0.001$). Compared with SAP, the mean morning glucose level (7:00 a.m.) was lower with CLC (123.7 vs 145.3 mg/dL; $P < 0.001$). The at-home substudy (n = 10) showed similar overnight trends, with increased time in target (70 to 180 mg/dL) for CLC vs SAP (75.2% vs 62.2%; $P = 0.07$) and decreased time in hypoglycemia (< 70 mg/dL) for CLC vs SAP (0.6% vs 3.7%; $P = 0.03$).

Conclusions

Overnight-only CLC increased the time with blood glucose readings within the target range and decreased the time in hypoglycemic range over 24 hours in a supervised outpatient setting. An at-home pilot extension study showed a similar nonsignificant trend.

Comment

Prior studies have shown the challenges of closed-loop control (CLC) during the daytime (13), particularly as it relates to the challenges of large meals affecting glycemic control. This study sought to optimize glycemic control by using CLC overnight, improving overnight time in range 70–180 mg/dL and overnight time < 70 mg/dL. Interestingly, 7 a.m. mean glucose improved from 145.3 to 123.7 mg/dL ($P < 0.001$), and this effect lasted throughout the day during the 5-day inpatient study, with time in range and percent time < 70 mg/dL improving throughout the 24-h period. These results confirm the benefits found in previous studies examining only overnight closed-loop control (14–16). In the 6-week MD-Logic closed-loop use at-home study, the lower morning fasting glucose levels achieved by the

system were found to have a positive effect on daytime glycemic control (17). This suggests overnight CLC may lead to improvements in glycemic control throughout the day as well, when CLC is not active. The pilot extension study, performed at home, also showed a significant improvement overnight, but a nonsignificant trend during the 24-h period, suggesting that the aforementioned challenges of large meals and other activities in the unsupervised environment during the daytime still present a challenge for CLC systems.

Closed-loop glucose control in young people with type 1 diabetes during and after unannounced physical activity: a randomised controlled crossover trial

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This manuscript is also discussed in the article on Advances in Exercise, Physical Activity, and Diabetes Mellitus, page S-112, and the article on Diabetes Technology and Therapy in the Pediatric Age Group page S-123.

Background

Adjusting treatment for exercise and avoiding hypoglycemia remains a significant hurdle for closed-loop systems. The present study evaluated the safety and efficacy of closed-loop insulin delivery during unannounced (to the closed-loop algorithm) afternoon physical activity and during the following night in young people with T1D.

Methods

Children and adolescents with T1D aged 10–17 years who were experienced insulin pump users were randomly assigned to perform physical activity for 2 consecutive days using either using closed-loop or open-loop insulin delivery in the inpatient setting, then switched to the other system for another 2 days. Subjects performed two unannounced exercise protocols: moderate intensity (55% of VO_2max) and moderate intensity with integrated high-intensity sprints (55/80% of VO_2max). Glycemic control was measured during the exercise period and the following night. For the open-loop insulin delivery control, the device was disconnected during exercise and the basal insulin dose was reduced by 20% for 4 h following the exercise session. During the closed-loop insulin delivery, the use of the pump was uninterrupted. Closed-loop insulin delivery was applied from 3:00 p.m. on the day of the exercise session to 1:00 p.m. on the following day, and exercise was not announced to the closed-loop algorithm.

Results

Twenty eligible participants (9 female, mean age 14.2 ± 2.0 years, HbA1c 7.7 ± 0.6% [60.0 ± 6.6 mmol/mol]) were included in the trial, and all completed the required activities. The median proportion of time spent in hypoglycemia of < 60 mg/dL [< 3.3 mmol/L] was 0.00% for both treatment modalities ($P = 0.79$). The proportion of time spent within the target glucose range of 70–180 mg/dL [3.9–10 mmol/L] increased with closed-loop compared with open-loop delivery: 84.1% (interquartile range 70.0–85.5) vs 68.7% (59.0–77.7), respectively ($P = 0.006$), over the entire study period. Closed-loop also delivered significantly less insulin than the open-loop system: 112.6 U (73.1–200.3 U) vs 203.7 U (91.6–277.1 U) ($P = 0.0123$). During the study, 6 hypoglycemic events were recorded in the closed-loop group and 12 in the open-loop group ($P = 0.516$); participants received rescue carbohydrates on 7 occasions in the closed-loop group (total of 105 g), and on 8 occasions in the open-loop group (total of 120 g).

Conclusions

Closed-loop insulin delivery was safe both during and after unannounced exercise protocols, maintaining glucose values mostly within the target range without an increased risk of hypoglycemia.

Comments

Exercise remains as a consistent challenge to closed-loop systems, as it is difficult to maintain within-range glucose levels after unannounced exercise of varying intensities. This study sought to determine whether closed-loop would outperform open-loop delivery after unannounced afternoon exercise, a challenging period linked with nighttime hypoglycemic events. In this study, use of the closed-loop system showed significantly more time in the target glucose range while delivering less total insulin. Hypoglycemia was treated in both groups, with a nonsignificant reduction in hypoglycemic events (6 total with 3 at night for closed-loop vs 12 total with 4 at night for open-loop). Additional studies are needed to demonstrate safety for exercise and closed-loop, particularly when used without any form of announcement (extra carbohydrates, reduced boluses, or user-initiated temporary basal rates prior to exercise).

Fully closed-loop multiple model probabilistic predictive controller artificial pancreas performance in adolescents and adults in a supervised hotel setting

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*Diabetes Technol Ther 2018; **20**: 335–343*

Background

Multiple model probabilistic predictive control (MMPPC) is a fully closed-loop system that uses probabilistic estimation of meals to allow for automated meal detection. This is in contrast to hybrid closed-loop systems that are designed to still require prandial meal announcements, which does not eliminate the burden of premeal insulin dosing. This study describes the safety and performance of the MMPPC system with announced and unannounced meals in a supervised hotel setting.

Methods

This 72-h test of the Android phone–based AP system with remote monitoring included 10 patients (6 adults and 4 adolescents) across three clinical sites using daily exercise and meal challenges involving three announced (manual bolus by patient) as well as six unannounced (no bolus by patient) meals. Controller aggressiveness was adapted daily based on prior hypoglycemic events.

Results

Mean 24-h CGM glucose was 157.4 ± 14.4 mg/dL, with 63.6 ± 9.2% of readings falling within the 70–180 mg/dL range, 2.9 ± 2.3% of readings < 70 mg/dL, and 9.0 ± 3.9% of readings > 250 mg/dL. Moderate hypoglycemia (glucose 180–250 mg/dL) was relatively common (24.6 ± 6.2% of readings) and usually occurred within 3 h following a meal. Overnight mean CGM was 139.6 ± 27.6 mg/dL, with 77.9 ± 16.4% of readings in the range of 70–180 mg/dL; 3.0 ± 4.5% under 70 mg/dL; 17.1 ± 14.9% between 180 and 250 mg/dL; and 2.0 ± 4.5% over 250 mg/dL. Postprandial hyperglycemia was more likely to occur after unannounced meals than after announced meals (4-h postmeal CGM 197.8 ± 44.1 vs 140.6 ± 35.0 mg/dL; $P < 0.001$). No participants met safety stopping criteria.

Conclusions

MMPPC was considered safe in a supervised setting despite meal and exercise challenges. Further studies in less-supervised situations are warranted.

Comments

Automatic detection and treatment of unannounced meals are significant challenges for current AP systems. Creating a system that could automatically detect and correct for postprandial hyperglycemia holds great potential to tremendously improve glucose control, as shown in an AP study with the Zone-MPC algorithm with 50-g carbohydrate unannounced meals (18). In this study with MMPPC use, the 4-h postmeal CGM averaged under 200 mg/dL for the unannounced meals, showing that this is the first step toward eventually eliminating the need for meal boluses, even with a single-hormone (insulin-only) AP system.

Impact of macronutrient content of meals on postprandial glucose control in the context of closed-loop insulin delivery: a randomized cross-over study

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*Diabetes Obes Metab 2018; **20**: 2695–2699*

Background

This study sought to examine the effect of added protein and/or fat in standard meals with a fixed carbohydrate content on postprandial glucose control with closed-loop insulin delivery in adults with T1D.

Methods

Meals were randomized in a four-way crossover study. Participants (n = 15) were given four different breakfast meals, all of which contained the same amount of carbohydrates (75 ± 1 g). Three of the breakfasts also included added protein and/or fat (35 ± 2 g). The four breakfast variations included (1) carbohydrate-only (standard), (2) high protein, (3) high fat, and (4) high fat/high protein.

Results

Insulin bolus and infusion rates were generated by the closed-loop insulin delivery algorithm. The main outcome was 5-hour postmeal sensor glucose area under the curve (AUC). The AUC was not affected by the addition of fat, protein, or both, nor were mean sensor glucose, or glycemic peak as compared with a standard meal ($P > 0.05$). The addition of both fat and protein was associated with a 40-min delay in time to glycemic peak ($P = 0.03$) and 39% higher 5-hour postmeal basal insulin requirements ($P = 0.04$) compared with a standard meal.

Conclusions

In the context of closed-loop insulin delivery, the protein and/or fat content of a meal affects the timing of postprandial glycemic peak, insulin requirements, and late glycemic excursion, without impacting overall 5-hour AUC.

Comment

Despite many closed-loop studies examining methods to improve efficacy, it is rare that meal macronutrient content is specifically reported and considered when treating postprandial hyperglycemia. The effects of different macronutrients on closed-loop response have not been commonly researched, making this study important for highlighting the topic. It was promising to see that different macronutrient contents for the study meals could be treated equally as well by the study closed-loop system, without compromising 5-hour AUC. The optimal treatment of high-fat and high-protein meals in the context of closed-loop insulin delivery remains to be determined, as well as how to best inform a closed-loop system of the meal macronutrient content.

Evaluation of an artificial pancreas with enhanced model predictive control and a glucose prediction trust index with unannounced exercise

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*Diabetes Technol Ther 2018; **20**: 455–464*

Background

This study investigated the safety and efficacy of the addition of a trust index to enhanced model predictive control (eMPC) artificial pancreas (AP). The trust index used no additional information than what is normally provided to the MPC controller (CGM readings, prior insulin delivery, basal profile, total daily insulin, body weight) but enhanced controller aggressiveness of insulin recommendations based on recent prediction error residuals (how accurate the model predictions were when looking back over the last few hours).

Methods

After 1 week of SAP use, subjects completed a 48-h AP admission that included three meals per day (containing 29–57 g carbohydrates per meal), a 1-h unannounced brisk walk, and two overnight periods. Endpoints included percentage time with sensor glucose of 70–180 mg/dL, <70 mg/dL, and >180 mg/dL; number of hypoglycemic events; and assessment of the trust index vs standard eMPC glucose predictions.

Results

Fifteen adult subjects (mean HbA1c 7.2% ±1.0%) completed the study. Mean sensor glucose percent time 70–180 mg/dL (88.0% ±8.0% vs 74.6% ±9.4%), <70 mg/dL (1.5% ±1.9% vs 7.8% ±6.0%), and number of hypoglycemic events (0.6±0.6 vs 6.3±3.4) all showed statistically significant improvement during AP use compared with the SAP run-in ($P<0.001$). On average, the trust index enhanced controller responsiveness to predicted hyper- and hypoglycemia by 26% ($P<0.005$).

Conclusions

eMPC with trust index AP achieved nearly 90% time in the target glucose range in a small cohort of patients in a 48-h study with close physician supervision.

Comments

Most AP systems work as a single input/single output system, taking input from the continuous glucose monitor and giving output of suggested insulin dosing. The trust index in this study worked by examining the results of prior future glucose predictions made by the controller and adapted up or down the responsiveness of the controller's suggested insulin changes based on how accurate the model predictions were. As there are many factors that could affect the accuracy of future glucose predictions (erroneous CGM readings, CGM calibrations, under- or overbolusing for carbohydrates, unannounced exercise, etc.), the trust index served as a way to prevent oscillations in blood glucose by pairing back controller responsiveness when trust in the prediction model was low, regardless of the underlying cause. In this study, time in the target glucose range 70–180 mg/dL increased to 88%, much higher than the baseline SAP run-in week, even for this well-controlled patient population. Larger studies in the unsupervised setting and in different populations are needed to validate these findings.

Ketone production in children with type 1 diabetes, ages 4–14 years, with and without nocturnal insulin pump suspension

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*Pediatr Diabetes 2017; **18**: 422–427*

Background

Elevated morning blood ketone levels are indicative of an insufficient nocturnal insulin supply. This study evaluated morning ketone levels in children with T1D following overnight use of an automated low-glucose insulin suspension system compared with control nights when the system was not used.

Methods

Morning blood ketone levels were assessed in 28 children ages 4–9 years and 54 youth ages 10–14 years using the Precision Xtra Ketone meter following a cumulative 1155 and 2345 nights, respectively. Repeated measures logistic regression models were used to compare age groups for blood ketone level elevation following control vs intervention nights.

Results

Morning blood ketone levels were elevated (≥ 0.6 mmol/L) following control nights for 10% of 580 nights in the 4- to 9-year-old group vs 2% of 1162 nights in the 10- to 14-year-old group ($P < 0.001$). A similar trend was seen following intervention nights in the younger cohort (13% of 575 nights vs 2% of 1183 nights; $P < 0.001$). In the younger age group, a longer duration of pump suspension resulted in a higher percentage of mornings with elevated blood ketones ($P < 0.002$), but this was not found in the older age group ($P = 0.63$). Ketoacidosis did not occur in any subjects.

Conclusions

Elevated morning blood ketones are more common in younger children with T1D, with or without nocturnal insulin suspension. Care providers need to be aware of the differences in ketogenesis in younger age children relative to various clinical situations.

Comments

Insulin deficiency resulting from insulin pump suspension, in this case occurring after automated suspension as part of a PLGS system, can lead to ketosis. This study is important because in it the 4- to 9-year-old age group had a substantially higher frequency of elevated morning ketones following both control nights and intervention nights, indicating that the effect was physiologically inherent with age and not related to system use. The clinical significance of morning ketones may be minimal, as all instances of ketones ≥ 1.0 mmol/L returned to normal within hours without incident. The incidence of elevated ketones in the 10- to 14-year age group was similar to that previously described for a 15- to 45-year age group (19,20). As such, providers should be aware this could occur, especially in younger children during times of illness, but overall these systems that automatically suspend and resume insulin delivery appear safe and effective.

Predictive hyperglycemia and hypoglycemia minimization: in-home double-blind randomized controlled evaluation in children and young adolescents

Forlenza GP[1], Raghinaru D[2], Cameron F[3], Bequette BW[3], Chase HP[1], Wadwa RP[1], Maahs DM[1,4], Jost E[1], Ly TT[4], Wilson DM[4], Norlander L[4], Ekhlaspour L[4], Min H[4], Clinton P[4], Njeru N[2], Lum JW[2], Kollman C[2], Beck RW[2], Buckingham BA[4]; for the In-Home Closed-Loop (IHCL) Study Group

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*Pediatr Diabetes 2018; **19**: 420–428*

Background

This study sought to compare the effectiveness of a predictive hyperglycemia and hypoglycemia minimization (PHHM) system vs predictive low glucose suspension (PLGS) alone in optimizing overnight glucose control in children 6–14 years old in double-blind study design.

Methods

Twenty-eight participants aged 6–14 years of age were randomized per night into PHHM mode or PLGS-only mode while at in-home settings. A total of 1290 randomized nights, with a median of 9.3 hours of sensor data per night, were included in the primary analysis. Primary outcome was the percent time sensor glucose was within range (70–180 mg/dL) during the overnight period.

Results

Time in target range (70–180 mg/dL) increased to $76 \pm 9\%$ during PHHM nights compared with $66 \pm 11\%$ during PLGS nights ($P < 0.001$), without increasing hypoglycemia. Average morning blood glucose also improved to 154 ± 19 mg/dL following PHHM nights as compared to 176 ± 28 mg/dL following PLGS nights ($P < 0.001$).

Conclusions

The PHHM system improved overnight glycemic control, significantly increasing time in range, lowering mean glucose, and decreasing glycemic variability as compared to PLGS alone in children 6–14 years old.

Comments

In a prior study, the PHHM system, an insulin-dosing module added to an existing PLGS algorithm, was tested in 30 participants who were 15–45 years old, with each participant using the system for 42 nights and randomization each night to have hyperglycemia mitigation active or inactive and PLGS active each night. The results of that trial demonstrated that PHHM significantly improved time in target range of 70–180 mg/dL by 7% and average morning glucose by 21 mg/dL when compared with PLGS alone (21). This study further supports these results, showing that in children 6–14 years old, use of the PHHM system gave superior results to PLGS alone, and is similar to results from other trials of AP supporting the use of automated insulin delivery systems for people with T1D.

SUMMARY

This year's studies demonstrate continued improvements in the efficacy of decision support systems and closed-loop

systems. A recent meta-analysis confirms these findings, noting that AP systems uniformly and similarly improve glucose control in outpatient settings compared with conventional or SAP therapy, despite variable clinical and technical characteristics (22). The use of closed-loop system increased time within range by 12.6% (95% CI 9%–16%), equivalent to nearly 3 hours per day. The convergence of glucose levels into the target range was a consequence of reduction of time in both hypoglycemia and hyperglycemia. This meta-analysis showed an estimated 50% reduction in relative risk for hypoglycemia. The data gathered also showed that the increase in time within range was greater in overnight studies than in studies done for day and night. This points out for the need to search for means to improve daytime control. Indeed, several methods have been tested and described in this article to overcome daytime obstacles: use of optimization support algorithms, implementation of sensors, medications, and more to empower the closed-loop decisions and performance. Although meta-analysis has its limitations, the data strongly point out the efficacy and safety of the closed-loop system to become the management choice for people with T1D in the near future.

Future studies will no doubt continue to evaluate efficacy of the systems studied in different populations and in different clinical scenarios. As more patients gain access to decision support systems in the future, either through supervised use by their medical provider or by unsupervised use at home, we may find decision support systems offer additional treatment modalities to a large number of patients. These systems may enable more accurate insulin dosing based on data gathered from patient's devices and give personalized recommendations to empower the patient's self-management, a feat that could improve access to health care, reduce clinical visits, and potentially increase diabetes treatment satisfaction and quality of life.

In addition, with more patients gaining access to commercially released closed-loop systems, a significant amount of data will be generated concerning how effective these systems are for real-world use.

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