Frontiers in Medical Case Reports, ISSN: 2582-8142

Insulin Delivery Utilizing Hybrid-Closed-Loop Therapy is More Effective When a Single Basal Rate Rather Than Multiple Basal Rates is Utilized - A Case Report

David S. H. Bell[1*] | Terri Jerkins[2]

***Correspondence:** David S. H. Bell

Address: [1]Southside Endocrinology - Birmingham, AL; [2]Midstate Endocrinology Associates – Nashville, TN

e-mail ✉: dshbell@yahoo.com

Received: 25 January 2022; **Accepted:** 02 February 2022

ABSTRACT

With Continuous Subcutaneous Insulin Infusion (CSII) multiple basal rates need to be utilized to avoid nocturnal hypoglycemia, the dawn phenomenon, postprandial hyperglycemia and preprandial hypoglycemia. With the availability of the Hybrid Closed-Loop Therapy (HCLT) systems, the use of multiple basal rates has become unnecessary and counterproductive. When transferring to a HCLT system we utilize a single basal rate for twenty-four hours. By utilizing a single basal rate we have improved multiple metrics of glycemic control in many patients. To illustrate the benefits of transfer to a single basal rate in a HCLT system we present a relevant case.

Keywords: *Continuous Subcutaneous Insulin Infusion, Hybrid Closed-Loop Therapy, Multiple Basal Rates, Single Basal Rate*

Introduction

When Continuous Subcutaneous Insulin Infusion (CSII) first became available in the early 1980s, CSII operated with a single basal rate (Tamborlane *et al*., 1979). Subsequently, CSII included the opportunity to utilize several basal rates which was initially discredited by some experts (Bell, 1994). However, it soon became obvious that to avoid nocturnal hypoglycemia, the dawn phenomenon, post-prandial hyperglycemia and pre-prandial hypoglycemia variable multiple basal rates were necessary and became "state of the art" (Bell, 1994).

With the availability of the Hybrid Closed-Loop Therapy (HCLT) systems, we transferred all patients with type 1 diabetes who were already utilizing a continuous glucose monitor and CSII to an HCLT system.

Our initial results were disappointing due to in most cases greater glycemic variability than had been present prior to utilizing the HCLT system and multiple adjustments of the basal rates, and bolus

insulin to carbohydrate ratios had little or no effect on this variability. However, an astute healthcare professional who was utilizing this system and had experienced these adjustment problems made the following observations:

1) the system worked better with a single low basal rate and
2) the system worked better when the sleep mode was disabled.

Based on this information, utilizing a single basal rate without a sleep mode achieved better glycemic outcomes. To illustrate this success we present a typical single case.

Case Presentation

A 42-year-old white female had had type 1 diabetes (Glutamic Acid Decarboxylase (GAD) positive, C-peptide less than 0.01 ng/ml) since age 9. She had utilized CSII for twelve years and still had poor glycemic control Hemoglobin A1c (HbA1c) 9.3% in spite of the use of nine basal rates and three pre-meal boluses in addition to many between meal boluses based on her continuous glucose monitor readings. When transferred to a HCLT system her glycemic control worsened (HbA1c over three months increased from 7.8% to 9.3%). On being transferred from her multiple basal rates to a single basal rate (0.6 units per hour which was her lowest basal rate) without the sleep mode multiple criteria of glycemic control improved significantly over five months as shown in Table 1. There were no changes in dietary therapy, mental health or social situation between stopping multiple basal rates and five months of utilizing a single basal rate.

Discussion

Hybrid closed-loop therapy is characterized by the coexistence of algorithm-driven automated insulin delivery combined with manual mealtime boluses (Leelarathna *et al*., 2021).

Prior to the availability of HCLT we treated with multiple basal rates to avoid nocturnal hypoglycemia, an early morning rise in glucose levels (dawn phenomenon which is probably delayed effect of growth hormone), postprandial hyperglycemia and preprandial hypoglycemia (Campbell *et al*., 1985). We also altered basal rates based on either home blood glucose monitoring by fingerstick or continuous monitoring of interstial fluid (CGM). Initially, CGM needed to be standardized with blood glucose monitoring, more recently this need has been waived (Grunberger *et al*., 2018). However, with the availability of HCLT readjustment of basal insulin doses became automatic based on CGM. However, pre-meal bolus insulin doses are delivered by the patients. Previous “real world” studies have shown that on transfer to HCL therapy time in range was significantly increased by 10.8% and time in hyperglycemia

range significantly reduced by 11.4% (Usoh *et al*., 2021).

We hypothesized that utilization of a single twenty-four-hour basal rate would not confuse the algorithm's ability to frequently adjust basal rates based on continuous glucose monitor readings and since correction boluses with HCLT can be administered as often as hourly, the use of more than one basal rate is at best superfluous. With regard to the sleep mode, we hypothesize that in this mode while the basal rates will be appropriately altered to avoid hypoglycemia, the hourly mini boluses used to correct hyperglycemia are not activated which can result in nocturnal hyperglycemia.

Therefore, to maximize the benefits of the HCLT systems based on this case and other cases that we have treated, we currently only utilize a single basal rate and avoid the use of the sleep mode. This, as shown in Table 1, has resulted in decreases in not only the HbA1c and average glucose levels but also the time in range. In addition, the standard deviation (a measure of glycemic variability) was remarkably reduced. Improvements in glycemic variability have been postulated to be a major factor in the reductions diabetic microvascular complications that is seen with better glycemic control (Brownlee and Hirsch, 2006).

Table 1: Glycemic metrics on changing to a single basal rate from multiple basal rates in a patient utilizing an HCLT system.

	PRE	POST
Date	05-06-2021	10-01-2021
HbA1c	9.30%	7.00%
Average Glucose	151 mg/dl	102 mg/dl
Range	70-180 mg/dl	70-180 mg/dl
Above 180 mg/dl	33%	19%
Above 240 mg/dl	43%	0%
Below 70 mg/dl	0%	1%
Below 50 mg/dl	0%	0%
Standard deviation	84 mg/l	49 mg/dl

While at this stage we recognize that we have only presented a preliminary clinical observation which is not based on prospective or even retrospective data, we nevertheless present our observation for the benefit of diabetic patients who are utilizing HCLT systems in addition to their endocrinologists and diabetologists. Currently we are embarking upon a large retrospective study involving a single large practice as well as a prospective study in another large practice where the single basal rate protocol has yet to be utilized in any of the many patients in that practice who are utilizing the HCLT systems.

Conclusion

Use of a single basal rate rather than multiple basal rates is more effective when HCLT is utilized.

References

Bell DSH. Insulin pump therapy for the 90's. *The Endocrinologist* 1994; 4: 270-278.

Brownlee M and Hirsch IB. Glycemic variability: a hemoglobin A1c-independent risk factor for diabetic complications. *JAMA* 2006; 295: 1707-1708.

Campbell PJ, Bolli GB, Cryer PE, Gerich JE. Pathogenesis of the dawn phenomenon in patients with insulin-dependent diabetes mellitus. Accelerated glucose production and impaired glucose utilization due to nocturnal surges in growth hormone secretion. *N Engl J Med* 1985; 312: 1473-1479.

Grunberger G, Handelsman Y, Bloomgarden ZT, Fonseca VA, Garber AJ, Haas RA, Roberts VL, Umpierrez GE. American Association of Clinical Endocrinologists and American College of Endocrinology 2018 Position Statement on Integration of Insulin Pumps and Continuous Glucose Monitoring in Patients with Diabetes Mellitus. *Endocr Pract* 2018; 24: 302-308.

Leelarathna L, Choudhary P, Wilmot EG, Lumb A, Street T, Kar P, Ng SM. Hybrid closed-loop therapy: Where are we in 2021? *Diabetes Obes Metab* 2021; 23: 655-660.

Tamborlane WV, Sherwin RS, Genel M, Felig P. Reduction to normal of plasma glucose in juvenile diabetes by subcutaneous administration of insulin with a portable infusion pump. *N Engl J Med* 1979; 300: 573-578.

Usoh CO, Johnson CP, Speiser JL, Bundy R, Dharod A, Aloi JA. Real-World Efficacy of the Hybrid Closed-Loop System. *J Diabetes Sci Technol* 2021; 11: 1932296820985103.