OBSERVATIONS

The Circadian Study:

The Get-Up Phenomenon in Type 1 Diabetes

Continuous subcutaneous insulin infusion (CSII) is the most advanced form of insulin administration in patients with type 1 diabetes. CSII can be initiated by one basal rate, providing the same amount of insulin every hour for the whole day, or by multiple basal rates providing a circadian variation of basal insulin with an increased infusion rate in the morning and evening hours (1). A circadian basal rate is considered to be closer to physiology and therefore to result in better glycemic control. Improved glycemia is thought to result mainly from an increase in insulin delivery in the early morning hours to antagonize the dawn phenomenon (2–4).

Individual adaptation of basal rates is time-consuming and frequently involves fasting tests. The better the starting basal rate fits the individual physiological basal insulin needs, the easier this procedure will be. The literature is sparse in terms of evidence of the importance of different starting basal rates. With this pilot trial, we established procedures and end points to demonstrate the feasibility of a large-scale trial that compares CSII therapy initiation and adaptation with different basal rate profiles.

The study included 12 adults with type 1 diabetes on CSII with A1C <8.5% and BMI <27 kg/m^2. Subjects were randomized 1:1 to the insulin pump therapy with one basal rate or multiple basal rates. During a structured therapy adaptation phase, subjects had scheduled standard meals and performed scheduled blood glucose measurements.

Mean 24-h blood glucose profiles during the adaptation period showed higher values in the one basal rate group, especially during daytime. Mean blood glucose levels for this period were 152 ± 8 mg/dl in the one basal rate group and 132 ± 9 mg/dl in the circadian group. Time outside the target BG range (70–140 mg/dl) was 10 h and 41 min in the one basal rate group vs. 7 h and 54 min in the circadian group.

We would like to highlight the following observation: subjects in the one basal rate group showed a blood glucose increase of 4.6 ± 6.4 mg/dl per hour between 4:00 A.M. and wake up and a more pronounced blood glucose increase of 26.6 ± 10.2 $mg \cdot dl^{-1} \cdot h^{-1}$ between getting up at 6:50 A.M. and breakfast (8:00 A.M.). We propose that the second blood glucose increase, previously referred to as the "rising phenomenon," should be named the "get-up phenomenon" (5). The get-up phenomenon is caused by starting morning activities and seems to have a more pronounced effect than the dawn phenomenon. In the circadian group, the dawn phenomenon and the get-up phenomenon were antagonized by the increasing basal rates, resulting in blood glucose decreases of 7.2 ± 4.3 and 19.5 ± 13.9 $mg \cdot dl^{-1} \cdot h^{-1}$, respectively.

In a large-scale trial, it will be interesting to further investigate the impact of the get-up phenomenon on achieving improved glycemia and optimizing insulin adaption procedures according to the individual morning activities.

GUIDO FRECKMANN, MD[1]
LOIS JOVANOVIC, MD[2]
ANNETTE BAUMSTARK, PHD[1]
CORNELIA HAUG, MD[1]
WIM VAN DER HELM, MD[3]

From the [1]Institute for Diabetes Technology at the University of Ulm, Ulm, Germany; the [2]Sansum Diabetes Research Institute, Santa Barbara, California; and [3]Disetronic Medical Systems AG, Burgdorf, Switzerland.

Corresponding author: Guido Freckmann, guido.freckmann@uni-ulm.de.

G.F. is a member of the Glucose Monitoring Study Group. L.J. has received a research grant from Roche Diagnostics Corporation and is a member of an advisory board for Roche Diagnostics Corporation.

DOI: 10.2337/dc08-1252. Clinical trial reg. no. 00569452, clinicaltrials.gov.

© 2008 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons.org/licenses/by-nc-nd/3.0/ for details.

Acknowledgments— This study was funded by Disetronic Medical Systems AG and was conducted by the team of the Institute for Diabetes-Technology at the University of Ulm.

References

1. Pickup J, Keen H: Continuous subcutaneous insulin infusion at 25 years: evidence base for the expanding use of insulin pump therapy in type 1 diabetes. *Diabetes Care* 25:593–598, 2002
2. Bolli GB, Gerich JE: The "dawn phenomenon"–a common occurrence in both non-insulin-dependent and insulin-dependent diabetes mellitus. *N Engl J Med* 22; 310:746–50, 1984
3. Koivisto VA, Yki-Järvinen H, Helve E, Karonen SL, Pelkonen R: Pathogenesis and prevention of the dawn phenomenon in diabetic patients treated with CSII. *Diabetes* 35:78–82, 1986
4. Carroll MF, Schade DS: The dawn phenomenon revisited: implications for diabetes therapy. *Endocr Pract* 11:55–64, 2005
5. Willms B, Wieland U: Das Aufstehphänomen. *Diabetes und Stoffwechsel* 3:229–232, 1994 [in German]

Downloaded from http://diabetesjournals.org/care/article-pdf/31/11/e85/596891/zdc01108000e85.pdf by guest on 03 October 2022