


Factors Associated With Glycemic Control During Free-Living Overnight Closed-Loop Insulin Delivery in Children and Adults With Type 1 Diabetes

Journal of Diabetes Science and Technology

2015, Vol. 9(6) 1346–1347

© 2015 Diabetes Technology Society 

Reprints and permissions:

sagepub.com/journalsPermissions.nav

DOI: 10.1177/1932296815604439

dst.sagepub.com



Martin Tauschmann, MD¹, Hood Thabit, MD¹, Lalantha Leelarathna, PhD¹, Daniela Elleri, PhD¹, Janet M. Allen, RN¹, Alexandra Lubina-Solomon, PhD², Marietta Stadler, PhD³, Emma Walkinshaw, MRCP², Ahmed Iqbal, MRCP², Pratik Choudhary, MD³, Malgorzata E. Wilinska, PhD¹, Simon R. Heller, FRCP², Stephanie A. Amiel, FRCP³, Mark L. Evans, FRCP¹, David B. Dunger, FRCP¹, and Roman Hovorka, PhD¹

Keywords

closed-loop insulin delivery, glycemic control, home study, predictive factors, type 1 diabetes

Unsupervised free-living overnight home use of closed-loop insulin delivery is feasible, safe, and effective in adolescents¹ and adults² with type 1 diabetes, but outcomes vary between individuals. Understanding factors influencing glucose outcomes may help to identify vulnerable populations, guide design of future studies, and lead to enhanced control algorithms.

To explore associations between demographic characteristics, the use of closed-loop and glucose performance, we pooled data from 2 multicenter trials, 1 involving adolescents,¹ and 1 involving adults² with type 1 diabetes. Both studies adopted an open-label, cross-over, randomized controlled study design. Participants were randomly assigned to 4 (adults) or 3 (adolescents) weeks of sensor-augmented pump therapy with or without overnight closed-loop. An identical model-predictive-control algorithm was used in both studies.³ Participants were instructed to start the system at home after their evening meal and to discontinue it before breakfast the next morning. Detailed methods and results are reported elsewhere.¹⁻²

In the present work, Pearson's correlation coefficients quantified the relationship between baseline demographic factors (age, BMI, HbA1c, total daily dose), participant-level utility characteristics (average duration of closed-loop application, average start time of closed-loop) and closed-loop outcomes between midnight and 08:00 (mean glucose, time in target between 70 and 145 mg/dl, time below 70 mg/dl) (Table 1). Age and time below target were rank-normal transformed. Associations with gender were evaluated applying Spearman correlation. Multiple linear regression analysis quantified the amount of explained variability of closed-loop outcomes using demographic and utility characteristics.

Forty participants completed the studies, including 24 adults (age 43 ± 12 years [mean \pm SD]; HbA1C 64.9 ± 8.9 mmol/mol, $8.1 \pm 0.8\%$; BMI 26.0 ± 3.5 kg/m²; total daily

insulin dose 0.5 ± 0.1 U/kg/day) and 16 adolescents (age 15.6 ± 2.1 years; HbA1C 63.9 ± 9.4 mmol/mol, $8.0 \pm 0.9\%$; BMI 22.4 ± 3.7 kg/m²; total daily insulin dose 0.8 ± 0.2 U/kg/day).

Data on 866 closed-loop nights were analyzed. HbA1c at baseline was associated with mean glucose during closed-loop nights ($r = .52$, $P = .001$) and time with hypoglycemia ($r = -.43$, $P = .006$), but not time in target ($r = -.26$, $P = .101$). Early closed-loop start and longer closed-loop application tended to increase time in target ($P = .064$). There was an age-associated reduction in time in target ($r = -.33$, $P = .038$), perhaps reflecting the association between older age and shorter period of closed-loop use ($r = -.58$, $P < .001$). Of the variance in mean glucose, 33% was explained by the regression model ($P = .028$), with HbA1c as the only significant predictor ($P = .001$). For time below target, the explained variance was 36% ($P = .017$); earlier closed-loop start time ($P = .017$) and HbA1c ($P = .008$) were significant predictors. Only 20% of variance in time in target was explained by the regression model.

The strength of the current work is that the data were collected during free-living unsupervised home closed-loop use. Weaknesses include that we did not capture at all or with low confidence other potentially influential factors such as

¹Wellcome Trust-MRC Institute of Metabolic Science, University of Cambridge, Cambridge, UK

²Academic Unit of Diabetes, Endocrinology and Metabolism, Department of Human Metabolism, University of Sheffield, Sheffield, UK

³Diabetes Research Group, King's College London, London, UK

Corresponding Author:

Roman Hovorka, PhD, University of Cambridge Metabolic Research Laboratories, Level 4, Institute of Metabolic Science, Box 289, Addenbrooke's Hospital, Hills Rd, Cambridge CB2 0QQ, UK.
Email: rh347@cam.ac.uk

Table 1. Pearson's Correlation Coefficients Between Closed-Loop Outcomes and Demographic and Utility Characteristics (N = 40).

	Age	BMI	HbA1c	Total daily dose	Duration of closed-loop application	Time of closed-loop start
Mean glucose (P value)	.17 (.294)	.10 (.550)	.52 (.001)	-.25 (.119)	-.20 (.209)	.25 (.117)
Time in target 70-145 mg/dl (P value)	-.33 (.038)	-.24 (.129)	-.26 (.101)	.27 (.097)	.30 (.064)	-.30 (.064)
Time below 70 mg/dl (P value)	.04 (.786)	.14 (.386)	-.43 (.006)	.06 (.702)	-.12 (.473)	-.25 (.127)

socioeconomic and educational status, exercise patterns, and meal size and composition.

In conclusion, in adolescents and adults with type 1 diabetes undergoing overnight closed-loop, baseline HbA1c is correlated with mean overnight glucose but not time in target range. Despite closed-loop, a lower HbA1c level remains a risk factor for nocturnal hypoglycemia. Improved time in target may be observed if overnight closed-loop is started earlier and applied for longer.

Abbreviations

BMI, body mass index; SD, standard deviation.

Acknowledgments

We are grateful to study volunteers for their participation. Professor Peter Hindmarsh (University College, London) helped in identifying potential recruits. We acknowledge support from the staff at the Addenbrooke's Wellcome Trust Clinical Research Facility, Sheffield's Centre for Biomedical Research Clinical Research Facility and the NIHR-Wellcome Trust King's Clinical Research Facility. Josephine Hayes (Institute of Metabolic Science, University of Cambridge) provided administrative support. Andrew Pernet, Bula Wilson, and Louisa Green provided clinical support at the research facility (Kings College London). Arti Gulati (University of Cambridge) provided data management support. Karen Whitehead (University of Cambridge) provided laboratory support. The Core Biochemical Assay Laboratory, University of Cambridge (Keith Burling) carried out biochemical analyses.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: PC declares speaker honoraria and travel support from Medtronic, Roche and Lifescan, and has undertaken consultancy for NovoNordisk and Eli Lilly, for which his institution has received payment. He has spoken at meetings for which he has received payment from NovoNordisk, Eli Lilly, and Beckton Dickinson. Medtronic has provided research support for some of his work. MEW reports receiving licensing fees from Beckton Dickinson. SRH has undertaken consultancy work for Novo Nordisk and Eli

Lilly, for which his institution has received payment. He has spoken at meetings for which he has received payment from NovoNordisk, Eli Lilly, and Beckton Dickinson. Medtronic has provided research support for some of his work. MLE has received speaker honoraria from Eli Lilly, Animas, and Abbott Diabetes Care and served on advisory panels for Medtronic, Roche, Sanofi-Aventis, and Cellnovo. MEW, DBD, and RH report patent applications. RH has received speaker honoraria from Minimed Medtronic, Lifescan, Eli Lilly, BBraun, and Novo Nordisk, serves on an advisory panel for Animas, Minimed Medtronic, and Eli Lilly, has received license fees from BBraun, Medtronic, and Beckton Dickinson, and has served as a consultant to Beckton Dickinson, BBraun, Sanofi-Aventis, and Profil. The other authors have no conflicting interests to declare.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Funding for these studies was received from the JDRF (#22-2009-802) and Diabetes UK (BDA07/0003549), with additional support for the Artificial Pancreas work by National Institute of Diabetes and Digestive and Kidney Diseases (1R01DK085621), Wellcome Strategic Award (100574/Z/12/Z), and National Institute for Health Research Cambridge Biomedical Research Centre. Abbott Diabetes Care supplied continuous glucose delivery devices and sensors and modified devices to facilitate real-time connectivity. No funder had any role in the study design, data collection/analysis/interpretation or manuscript preparation.

References

1. Hovorka R, Elleri D, Thabit H, et al. Overnight closed loop insulin delivery in young people with type 1 diabetes: a free-living randomised clinical trial. *Diabetes Care*. 2014;37:1204-1211.
2. Thabit H, Lubina-Solomon A, Stadler M, et al. Home use of closed-loop insulin delivery for overnight glucose control in adults with type 1 diabetes: a 4-week, multicentre, randomised crossover study. *Lancet Diabetes Endocrinol*. 2014;2:701-709.
3. Elleri D, Allen JM, Biagioni M, et al. Evaluation of a portable ambulatory prototype for automated overnight closed-loop insulin delivery in young people with type 1 diabetes. *Pediatr Diabetes*. 2012;13:449-453.