

Meta-Analysis of Overnight Closed-Loop Randomized Studies in Children and Adults with Type 1 Diabetes: The Cambridge Cohort

Kavita Kumareswaran, M.B.Ch.B.,^{1,2} Daniela Elleri, M.D.,^{1,3} Janet M. Allen, R.N.,^{1,3} Julie Harris, R.N.,¹ Dongyuan Xing, M.P.H.,⁴ Craig Kollman, Ph.D.,⁴ Marianna Nodale, M.Sc.,¹ Helen R. Murphy, M.D., FRCP,¹ Stephanie A. Amiel, M.D., FRCP,⁵ Simon R. Heller, M.D., FRCP,⁶ Malgorzata E. Wilinska, Ph.D.,^{1,2} Carlo L. Acerini, M.D., FRCP,^{1,3} Mark L. Evans, M.D., FRCP,^{1,2} David B. Dunger, M.D., FRCP,^{1,3} and Roman Hovorka, Ph.D.^{1,3}

Abstract

Aim:

We reviewed the safety and efficacy of overnight closed-loop insulin delivery compared with conventional continuous subcutaneous insulin infusion (CSII) in two distinct age groups with type 1 diabetes mellitus (T1DM), young people aged 5 to 18 years and adults, combining data of previously published randomized studies.

Methods:

We evaluated four randomized crossover studies in 17 children and adolescents [13.4 ± 3.6 years; mean \pm standard deviation (SD)] and 24 adults (37.5 ± 9.1 years) on 45 closed-loop (intervention) and 45 CSII (control) visits. Each subject attended for two overnight study visits, using either closed-loop or conventional pump therapy, in random order. In each age group, studies were designed to mimic realistic likely scenarios. In the children and adolescent studies, closed loop was used following a standard evening meal and following 40 min of moderate-intensity exercise. In the adult studies, closed loop was commenced following a 60 g carbohydrate meal or a 100 g carbohydrate meal accompanied by alcohol. The primary outcome measure was time for which plasma glucose was within target range (3.91–8.0 mmol/liter).

Results:

Overnight closed loop increased the time in target plasma glucose in both young (from 40% to 60%, $p = .002$) and adults (from 50% to 76%, $p < .001$) compared with conventional CSII. Combined analysis showed an increase from 43% to 71% with closed loop ($p < .001$). Additionally, closed loop reduced the time spent below 3.91 mmol/liter and above 8.0 mmol/liter, from 4.1% to 2.1% ($p = .01$) and 33% to 20% ($p = .03$), respectively. Glycemic variability, as measured by the SD of plasma glucose, was lower during closed loop compared with CSII (1.5 versus 2.1 mmol/liter, $p = .007$).

continued →

Author Affiliations: ¹Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom; ²Department of Medicine, University of Cambridge, Cambridge, United Kingdom; ³Department of Pediatrics, University of Cambridge, Cambridge, United Kingdom; ⁴The Jaeb Center for Health Research, Tampa, Florida; ⁵Diabetes Research, King's College, London, London, United Kingdom; and ⁶Diabetes Centre, Clinical Sciences Centre, Northern General Hospital, Sheffield, United Kingdom

Abbreviations: (CGM) continuous glucose monitoring, (CHO) carbohydrate, (CSII) continuous subcutaneous insulin infusion, (CV) coefficient of variation, (GRT) Guardian REAL-Time, (SD) standard deviation, (T1DM) type 1 diabetes mellitus

Keywords: adults, alcohol, closed loop, exercise, large meal, young

Corresponding Author: Roman Hovorka, Ph.D., Institute of Metabolic Science, University of Cambridge, Box 289, Addenbrooke's Hospital, Hills Rd., Cambridge CB2 0QQ, UK; email address rh347@cam.ac.uk

Abstract cont.

Conclusions:

Overnight closed loop may improve glycemic control and reduce nocturnal hypoglycemia in both young people and adults with T1DM.

J Diabetes Sci Technol 2011;5(6):1352-1362