

Closed-Loop System Improves Glucose Control

BY MIRIAM E. TUCKER

A closed-loop system linking continuous glucose measurements to insulin delivery reduced the risk of nocturnal hypoglycemia compared with standard continuous subcutaneous insulin infusion in a three-part randomized crossover study involving 17 children and adolescents with type 1 diabetes.

Previous studies have assessed the feasibility of closed-loop systems using various types of control algorithms, but this is the first to compare closed-loop delivery with traditional continuous subcutaneous insulin infusion (CSII) and the first to assess the effect of evening meals and exercise, said Dr. Roman Hovorka of the University of Cambridge, England, and his associates (Lancet 2010 Feb. 5 [doi:10.1016/S0140-6736(09)61998-X]).

"Closed-loop systems could transform management of type 1 diabetes, but their introduction is likely to be gradual, starting from straightforward applications such as shutting off the pump at low glucose concentrations or overnight closed-loop delivery, proceeding to more complex applications providing 24-[hour] control," the investigators said.

The study subjects were aged 5-18 years and had type 1 diabetes for a mean duration of 6.4 years. Thirteen of the children were assigned to be treated with overnight (8:00 p.m. to 8:00 a.m.) closed-loop delivery (using Medtronic's Guardian Real-Time) or standard CSII on two separate occasions. Seven of those 13 were

VITALS

Major Finding: Compared to continuous insulin infusion, a closed-loop insulin delivery system increased the time plasma glucose was in the target range (60% vs. 40%) and significantly reduced the time in the hypoglycemic range (2.1% vs. 4.1%).

Data Source: A three-part randomized crossover study of 17 children and adolescents with type 1 diabetes.

Disclosures: Funding by the Juvenile Diabetes Research Foundation and three European research foundations. Dr. Hovorka has received lecture fees from Minimed Medtronic, Abbott Diabetes Care, Lifescan, Novo-Nordisk, and B. Braun. He reported two patent applications. Dr. Renard stated he had no conflicts of interest.

evaluated overnight with the closed-loop device (Abbott's Freestyle Navigator) on two further occasions, this time after having consumed either rapidly or slowly-absorbed large meals matched for total carbohydrates (129 grams), but differing in glycemic load.

In a third overnight evaluation, 10 adolescents aged 12-18 (including 4 from the first evaluation) rode a treadmill from 6:00 to 6:45 p.m. after having eaten a light meal at 4:00 p.m., again comparing closed loop (Navigator) with CSII. (All patients used Smiths Medical's Deltec Cosmo insulin pumps for the study.)

During closed-loop nights, glucose measurements were fed every 15 minutes into a control algorithm calculating rate of insulin infusion, and a nurse adjusted the insulin pump. Standard pump settings were used on control nights.

Primary outcomes—time for which plasma glucose concentration was in the target range of 3.91-8.00

mmol/L (70.4-144 mg/dL) or a hypoglycemic level of 3.90 mmol/L (70.2 mg/dL) or lower—did not differ significantly between closed loop and CSII for the first evaluation. Time spent in target range was 52% with closed loop versus 39% for CSII, and time spent with hypoglycemia, 1.0% vs. 2.0%. For the exercise evaluation, the proportions for closed loop vs. CSII were 78% vs. 43% of time in target range and 10.0% vs. 6.1% of time with hypoglycemia, respectively.

For the meal comparison, there was no significant difference in overnight control between the two meals: Time spent in target range after midnight was 86% for the rapidly-absorbed meal and 83% for the slowly absorbed meal. From the start of the closed-loop delivery, those proportions were 53% and 55%, respectively, Dr. Hovorka and his associates reported.

In a secondary analysis pooling the data from the first and third evaluations, closed-loop delivery significantly increased the time for which plasma glucose was in the target range (60% vs. 40%) and significantly reduced the time in hypoglycemic range (2.1% vs. 4.1%). The difference was even more significant after midnight, when closed-loop became fully effective (79% vs. 35% in target range, 3.0% vs. 6.1% hypoglycemic), they said.

In an accompanying editorial, Dr. Eric Renard of Université de Montpellier, France, commented that although overall mean blood glucose levels were not significantly different with closed-loop delivery, the fact that the closed loop stabilized blood glucose levels overnight while keeping hypoglycemia to a minimum is "an important step forward for young patients and their parents."

Exercise Improves CV Risk Markers in Diabetes

BY MARY ANN MOON

A 4-month exercise program of moderate intensity improved the inflammatory milieu, including markers of atherosclerosis, in overweight, sedentary diabetic patients.

The exercise did not alter body weight or insulin resistance, but it significantly improved glycemic, lipid, and cardiorespiratory factors, report-

ed Dr. Nikolaos P.E. Kadooglou of Hippokratia General Hospital of Thessaloniki (Greece) and his associates (Diabetes Metab. 2010 Feb. 9 [doi:10.1016/j.diabet.2009.11.004]).

The participants were randomly assigned to an exercise program or a control group. Subjects were instructed to perform 30-60 minutes of brisk walking at least 4 days per week, with no more than 2 consecutive days of inactivity. They also were encouraged to increase daily activities by taking walking breaks during the

work day, gardening, and doing household work. They were asked to meet with a personal trainer once a week for a 1-hour supervised session of aerobic activity.

A total of 87% of the patients in the exercise group said they achieved their target of 150 minutes per week of moderate-intensity exercise.

After 4 months, the exercise group had significantly increased exercise capacity, reduced hemoglobin A_{1c} levels, decreased BP, and lower levels of total and LDL cholesterol, whereas the control group did not. But there was no improvement in either group in body mass index, waist-to-hip ratio, insulin resistance, and MMP-2 and TIMP-1 levels, Dr. Kadooglou and colleagues wrote. ■

VITALS

Major Finding: Exercisers showed beneficial changes in MMP-9 levels and MMP9/TIMP ratios, compared with controls. Neither group improved in MMP-2 and TIMP-1 levels.

Data Source: Fifty overweight, sedentary type 2 diabetes patients randomized to exercise or no-exercise groups for 4 months.

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ed Dr. Nikolaos P.E. Kadooglou of Hippokratia General Hospital of Thessaloniki (Greece) and his associates (Diabetes Metab. 2010 Feb. 9 [doi:10.1016/j.diabet.2009.11.004]).

They compared outcomes in 50 sedentary, overweight, white patients with type 2 diabetes who were aged 50-65 years and whose glycemic control had failed to improve after they

High Coffee Intake Cuts Diabetes Risk 67% in American Indians

BY SHARON WORCESTER

Drinking 12 or more cups of coffee daily was associated with a significant reduction in the incidence of type 2 diabetes over nearly 8 years, compared with consuming no coffee, according a study.

The study looked at the self-reported coffee intake of the 4,579-person Strong Heart Study, an investigation of cardiovascular disease in 13 American Indian tribes/communities. Participants in that study had baseline data collected during 1989-1992 and were followed for an average of 7.6 years.

Participants in the current analysis were the 1,141 men and women who had normal fasting glucose at baseline, wrote Dr. Ying Zhang of the Oklahoma University Health Sciences Center, Oklahoma City, and associates (Nutr. Metab. Cardiovasc. Dis. 2009; Feb. 18 2010 [doi:10.1016/j.numecd.2009.10.020]).

The 92 (8.1%) participants who reported drinking at least 12 cups of coffee daily had a 67% lower risk (hazard ratio, 0.33) of developing type 2 diabetes during the follow-up period than did non-coffee drinkers, even after adjustment for age, gender, smoking, alcohol use, family history of diabetes, physical activity, and body mass index, the researchers noted.

In fact, coffee consumption was significantly related to diabetes risk only in those people who drank 12 or more cups daily.



A dozen cups of coffee or more per day yielded significant risk reduction.

The findings support those from several other studies showing a link between caffeine intake and diabetes development, but this is one of the few investigations that focused on a population known to have a high incidence of diabetes and on a group that, at baseline, had normal glucose tolerance.

The study was limited by a lack of available dietary data on the participants. It is plausible that high coffee consumption is a marker for dietary patterns and factors related to diabetes risk but not measured in this study, Dr. Zhang and associates noted.

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