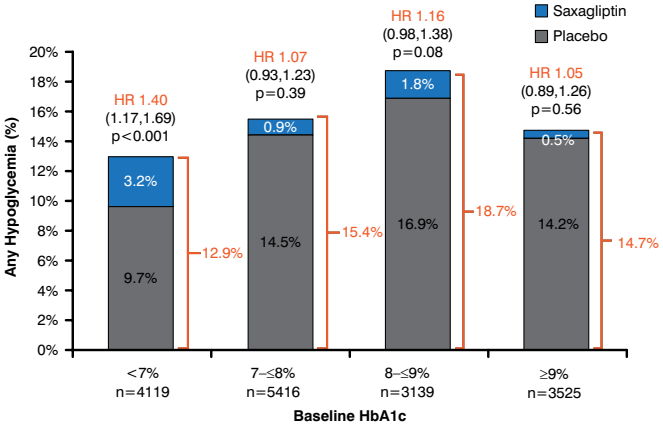
Figure 1. Effect of Saxagliptin on Hypoglycemic Events in SAVOR-TIMI 53



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Major episodes of major hypoglycemia were significantly increased in those patients with a baseline HbA1C <7% who were taking a sulfonylurea. Adding saxagliptin to conventional therapy for T2DM increased the proportion of patients whose HbA1C levels were reduced and glycemic targets achieved without hypoglycemic episodes.

Day and Night Closed-Loop Glucose Control Is Feasible in Type 1 Diabetes

Written by Emma Hitt Nichols, PhD

Twenty-four-hour glucose control using a closed-loop system was feasible and resulted in improved glucose control without increasing hypoglycemic events, according to data presented by Lalantha Leelarathna, PhD, University of Cambridge, Cambridge, United Kingdom, from the Closing the Loop in Adults With Sub-optimally Controlled Type 1 Diabetes Under Free Living Conditions study [AP@home02; NCT01666028]. The purpose of the AP@home02 study was to determine the feasibility of using a closed-loop insulin delivery system, combining an insulin pump and continuous glucose monitoring (CGM), for glucose control for 7 days in patients with type 1 diabetes mellitus (T1DM).

In this multinational (3 centers) crossover study, 17 (7 women) adult patients with T1DM were randomly assigned to open-loop or closed-loop glucose control for 7 days and then crossed over to the other modality for another 7 days. Prior to each at-home monitoring period, patients were monitored at the Clinical Research Center (CRC) for 23 hours. All patients received training on CGM and the closed-loop system during the run-in period.

The mean age of the study patients was 34 years, body mass index was 26.2 kg/m^2, and HbA1C was 7.6%. The mean duration of diabetes was 19 years, mean total daily insulin was 40.1 U, and total daily insulin per kilogram per day was 0.53 U.

In the CRC, patients had regular venous sampling, and insulin was given as a bolus 15 minutes before meals using a pump bolus calculator. No bolus was given for snacks during visits for the closed-loop system. At home and work, patients used the closed-loop system without supervision, but 24-hour telephone support was available.

The primary endpoint of glucose within the target range of 3.9 and 10.0 mmol/L during home use was achieved by 75% of patients during the closed-loop phase (95% CI, 62 to 82) compared with 63% during the open-loop phase (95% CI, 55 to 72; p = .006). Mean glucose levels were 8.1 mmol/L in the closed-loop arm compared with 8.8 mmol/L in the open-loop arm (p = .027). When stratified by time of day, the closed-loop system resulted in a greater amount of time in target glucose for both daytime (73%; 95% CI, 63 to 79) and nighttime (48%; 95% CI, 33 to 65) compared with the open-loop system (daytime, 65%; 95% CI, 55 to 71; p = .017; and nighttime, 35%; 95% CI, 28 to 48; p = .013). Insulin infusion with both systems during the home phase is detailed in Table 1.

Table 1. Insulin Infusion With the Closed-Loop and Open-Loop Systems During Home Phase

	Closed-Loop System	Open-Label System	p Value
Total daily insulin (U)	39.1	44.7	0.109
Total daily basal insulin (U)	20.1	18.9	0.017
Total daily bolus insulin (U)	18.9	26.5	0.002
SD of basal insulin (U)	0.7	0.2	< .001

SD = standard deviation.

In the utility analysis, the closed-loop system was operational 83% of the time during the home phase and 98% during the inpatient stay. Undesirable stopping of the closed-loop system occurred due to lack of pump connectivity or CGM availability, the user changing the pump settings, or other unknown reasons.

Adverse events included two severe hypoglycemic episodes; neither was during closed-loop operation, and both patients fully recovered. In one case, the sensor was not working. Four episodes of high glucose occurred because of failure of the insulin infusion system, but there was no ketosis or hospital admission.

In conclusion, Dr. Leelarathna stated these data suggest that day and night closed-loop glucose control is feasible to perform at home and may result in improved glucose control. Next, they will compare a closed-loop system and optimized sensor-augmented pump therapy in 30 patients at home for day and night control.

BF Reduces Risk of Diabetes After Gestational Diabetes

Written by Emma Hitt Nichols, PhD

Intensive breastfeeding (BF) decreased the risk of developing diabetes for women within 2 years after experiencing gestational diabetes mellitus (GDM) compared with exclusive formula feeding (FF). Erica P. Gunderson, PhD, MS, MPH, Senior Research Scientist, Kaiser Permanente, Oakland, California, USA, presented these data from the Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy study [SWIFT; R01 HD050625, Gunderson PI].

The few studies of outcomes of BF after GDM pregnancy have reported conflicting results, likely because of reverse causation or residual confounding, such as recall bias, the influences of other healthy lifestyle behaviors closely related to lactation, differences in GDM severity and treatment, and adverse perinatal outcomes that may determine lactation success. The purpose of the SWIFT study was to evaluate the effect of lactation on the progression to diabetes in women with a recent GDM pregnancy. The study was designed to evaluate and control for potential sources of reverse causation or residual confounding.

In the multicenter, prospective, observational study of 1035 women with GDM enrolled between 2008 and 2011, participants consented to 3 in-person exams within 2 years that included 2-hour 75-g oral glucose tolerance tests (OGTTs), received 10 monthly mailings throughout the first year, and participated in 3 telephone interviews (at >32 weeks gestation, and at 1 and 6 months postpartum). Women aged 20 to 45 years were eligible if they had a singleton, live birth at ≥35 weeks of gestation; were free of diabetes at 6 to 9 weeks postpartum; did not have preexisting diabetes; were not planning another pregnancy within 2 years; and were either intensively BF or FF at enrollment. The study population was racially and ethnically diverse; 24% were white, 31% Hispanic, 8% black, and 36% Asian.

The primary outcome was incident diabetes as measured by a 2-hour, 75-g OGTT. Lactation measures were quantitative and included intensity at baseline, which was 6 to 9 weeks postpartum, and subsequent monthly assessments of intensity and duration of BF and FF during the 2-year follow-up. Covariates included prenatal clinical outcomes, maternal and infant perinatal outcomes, and anthropometric measures, sociodemographics, and postpartum lifestyle behaviors.

The study classified women into four infant-feeding-intensity groups at 6 to 9 weeks postpartum: exclusive BF, mostly BF (<6 oz formula per day), high FF (>17 oz per day with some breast milk), and exclusive FF. There was no significant difference in prenatal 100-g OGTT results for women by BF or FF-intensity groups. Intensive BF (mostly or exclusive) was reported by 72%, 67%, and 54% of women at 1, 2, and 4 months postpartum, respectively. In addition, there were no significant differences in family history of diabetes, GDM treatment, gestational age, or prenatal 3-hour OGTT z-score among the breastfeeding intensity groups or the breastfeeding duration groups (0 to 2 months, 2 to <6 months, 6 to 14 months, and >14 months).

Compared with women who exclusively formula feed, the risk of developing diabetes within 2 years after delivery was lower with increasing BF intensity at 6 to 9 weeks postpartum, starting with high FF and some breast milk (HR, 0.61; 95% CI, 0.34 to 1.08), mostly breastfeeding (HR, 0.66; 95% CI, 0.41 to 1.07), to the lowest risk for the exclusively breastfeeding group (HR, 0.39; 95% CI, 0.22 to 0.77), after adjustment for race and ethnicity, prepregnancy body mass index, prenatal 3-hour OGTT z-score, and GDM treatment (trend p=.04). Lower risk of incident diabetes within 2 years postpartum was also associated with increasing duration of BF, with greatest benefit experienced by women who breastfed for >14 months compared with women who breastfed for 0 to 2 months in the fully adjusted model (p=.045; Table 1).

Table 1. Effect of Duration of Breastfeeding on Diabetes Incidence Within 2 Years After Gestational Diabetes

Models	0 to 2 Months	>2 to <6 Months	6 to 14 Months	>14 Months	p Value
	n=193	n=210	n=376	n=181	
Unadjusted	1.00	0.78	0.57	0.40	0.02
Adjusted[a]	1.00	0.86	0.70	0.47	0.13
Fully adjusted[b]	1.00	0.75	0.59	0.42	0.045

BMI=body mass index; GDM=gestational diabetes mellitus; OGTT=oral glucose tolerance test.

[a]Adjusted for prepregnancy BMI; [b]fully adjusted for prepregnancy BMI, prenatal 3-hour OGTT z-score, and GDM treatment.

The risk of developing diabetes after GDM was reduced with a longer duration of intensive BF in the SWIFT study.