Effectiveness of Continuous Glucose Monitoring in Pregnant Women with Diabetes: Randomised Clinical Trial


Purpose

- To evaluate the effectiveness of continuous glucose monitoring (CGM) during pregnancy on maternal glycemic control, infant birth weight, and the risk of macrosomia in women with type 1 and type 2 diabetes.

Endpoints

- The primary endpoint was maternal glycemic control during the second and third trimesters from measurements of HbA1c levels every four weeks.
- Secondary outcomes included birth weight and the risk of macrosomia based on the standard deviation scores of birthweight and customized birthweight centiles.

Methods

- The study had a prospective, open-label, randomized, controlled design. The study compared current prenatal care using self monitoring of blood glucose (SMBG) with prenatal care using a professional Continuous Glucose Monitoring System (CGMS) (Medtronic Minimed CGMS® Gold™).
- Study inclusion criteria were women who were pregnant, who were between the ages of 16-45 with type 1 or type 2 diabetes, and who were willing to wear a CGM monitor. Exclusion criteria included severe medical or psychological comorbidity. No women were excluded.
- CGM was offered for up to 7 days at intervals of 4-6 weeks between 8 and 32 weeks of gestation. The women removed the sensors 5-7 days after insertion. Data were downloaded to a personal computer using software (Medtronic Com-station, version 1.7B).
- Women were advised to perform at least 7 fingersticks per day. The subjects were provided with the following targets: 3.5-5.5 mmol/L (63-99 mg/dL) before meals, <7.8 mmol/L (<140 mg/dL) one hour after meals, and <6.7 mmol/L (<120 mg/dL) two hours after meals. SMBG results were verified using memory-based reflectance meters.
- Women were seen every 2-4 weeks for up to 28 weeks, every two weeks until 32 weeks, and weekly thereafter. Fetal growth assessments were performed at 28, 32, and 36 weeks. HbA1c levels were measured once every 4 weeks.
- Short-acting insulin analogs were used before meals along with intermediate acting insulin analogs, long-acting analogs, or insulin pump therapy. Women with type 2 diabetes were treated with insulin before pregnancy or as soon as pregnancy was confirmed.
- Intravenous infusions of glucose and insulin were used during labor and delivery, with blood glucose levels monitored hourly.
- The following definitions were used: macrosomia as a birth weight on or above the 90th centile, extremely large for gestational age as a birth weight on or above the 97.7th centile, and small for gestational age as a birth weight on or below the 10th centile.
- Birthweight standard deviation scores were calculated for only healthy single infants using the British 1990 growth standards; twins were excluded. Customized birthweight centiles were calculated using the open-source gestation network (GROW) program.

Results

- A total of 71 women with type 1 and type 2 diabetes participated in the study; 46 subjects (65%) had type 1 diabetes and 25 subjects (35%) had type 2 diabetes. Thirty-eight women were included in the CGM group and 33 women comprised the control group.
- At the beginning of the study, mean HbA1c levels were 7.3% ± 1.2% and mean gestational age was 9.2 ± 2.7 weeks. No significant differences were found between the groups except for the duration of diabetes, which was greater in the intervention (CGM) group.
- At the start of the study, the mean age was 31.3 ± 6.1 years, the mean body mass index was 28.1 ± 7.4, and the mean duration of diabetes was 12.8 ± 0.3 years.
The CGM device was generally well tolerated. Two pregnancies ended prematurely (one miscarriage and one termination). Two withdrew citing discomfort or dislike of the monitor. The mean number of periods of CGM for the remaining 36 women was 4.2 (range 0-8), with 29 (80%) of the subjects wearing the monitor at least once per trimester.

Glycemic Control

- HbA1c levels were consistently lower in the intervention arm. There was no statistical difference found in the mean levels between the two groups on enrollment or throughout the first two trimesters.
- Differences began to emerge between 28 and 32 weeks of gestation. Mean HbA1c levels in the CGM group were 6.1% ± 0.6% compared with 6.4% ± 0.8% in the control group, with a trend towards, but not reaching statistical significance (p=0.10).
- Differences in maternal HbA1c levels did reach statistical significance after 32 weeks, as the HbA1c levels for the CGM group continued to decline, while there was no further reduction in the control group. There was a difference in mean HbA1c levels of 0.6% between the two groups: 5.8% ± 0.6% in the CGM group compared with 6.4% ± 0.7% in the control group (p=0.007).

Pregnancy Outcomes

- From the 71 pregnancies, there were 69 infants born. There were 5 healthy twins (one twin had anencephaly), all in the CGM group. Two infants had malformations: one cardiovascular (in the control group) and one chromosomal (in the CGM group).
- Two-thirds of the deliveries were by Caesarean section with no difference between groups in the main gestational age at delivery. There was a trend towards reduced emergency Caesarean section in the CGM group (p=0.08).
- Neonatal morbidity was relatively uncommon. 17.4% (n=12) of the births were preterm deliveries, 21.7% (n=15) of infants were admitted to neonatal care, and 11.6% (n=8) of infants had hypoglycemia. There were no significant differences found between the groups.

Birth Weight

- Women in the CGM group had decreased mean birthweight standard deviation scores (0.9 vs. 1.6, p=0.05).
- The median birthweight centiles were 69% in the CGM group compared with 93% in the control group (p=0.02). The difference in birth weight centiles remained significant after exclusion of the 5 twins (p=0.04).
- In total, 31 of 67 infants (46%) were macrosomic. Thirteen of 37 infants (35%) in the CGM group were macrosomic compared with 18 of 30 infants (60%) in the control group. The odds ratio for reduced risk of macrosomia was 0.36 (p=0.05).
- Fewer extremely large for gestational age infants were born to mothers in the CGM group. In total, 5 of 37 (13.5%) births were classified as extremely large in the CGM group compared with the control group, which had 9 of 30 (30%) births classified in this manner. This difference did not reach statistical significance (p=0.13).
- The 2 largest infants born to mothers in the intervention arm were born to mothers who withdrew from the intervention (included in intent-to-treat and analysis).
- Four of 37 infants (10.8%) in the CGM group were small for gestational age compared with 0 of 30 infants in the control group (p=0.10). Formal testing showed that the number in the CGM group was no different than expected (11% vs. 10%, p=1.0).

Conclusions

- The use of supplementary CGM as an educational tool during pregnancy was associated with improved glycemic control and reduced risk of macrosomia.
- Improvements in glycemic profiles were achieved gradually over time, underscoring the importance of using CGM over several visits for better results.
- Initiating CGM earlier in the pregnancy (ideally prior to conception) may help to achieve an earlier impact on glycemic control.

*Adapted from study.