Non–Glycemic-Dependent Reduction of Late Pregnancy A1C Levels in Women With Type 1 Diabetes

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A reduction of A1C levels during pregnancy in women without diabetes has been reported (1–6), suggesting that the goal for A1C during pregnancy complicated with diabetes should be lowered. The decrease in fasting blood glucose levels during the first trimester of normal pregnancy (7,8) may explain the lower A1C levels found in early pregnancy (1,2,3,5). A further decrease of A1C in late pregnancy in women without diabetes has been reported by Nielsen et al. (3), which may be related to decreased erythrocyte life span (9,10).

In women with type 1 diabetes, strict glycemic control during pregnancy leads to a reduction in A1C levels, which may be insufficient to prevent the complications of pregnancy in type 1 diabetes (11,12). Since the decrease in A1C during normal pregnancy is related to lower blood glucose and to decreased erythrocyte lifespan (6–10), some of the reduction of A1C observed in pregnant women with type 1 diabetes will not be related to improved glycemic control. Therefore, A1C levels in pregnancies complicated by diabetes can be misleading when evaluating the degree of glycemic control. The aim of this study was to quantify the decrease in A1C levels during late pregnancy in women with type 1 diabetes who were not dependent on glycemic control.

RESEARCH DESIGN AND METHODS

— This study was performed at the Hospital Universitario La Paz, Madrid, Spain. Ethical approval for this research was provided by the hospital's ethical committee, and all women gave their informed consent.

From our Diabetes and Pregnancy Unit, we selected 68 women with type 1 diabetes, aged 32.0 ± 3.0 years, with diabetes duration 14.6 ± 7.5 years and prepregnancy BMI 24.6 ± 3.4 kg/m^2, who performed home blood glucose monitoring using the same type of glucose meter (OneTouch profile; LifeScan, Milpitas, CA) from at least 3 months before conception and throughout pregnancy. All women were on flexible basal bolus insulin regimens and were trained to adjust their insulin dose.

Glucose readings stored in the meter were downloaded to a computer (diabetes management software In Touch; LifeScan) at each visit. Mean glucose levels were obtained from the glucose readings for the 12 weeks before conception (preconception) and for the third trimester (from 25 gestational weeks to 36 complete gestational weeks). The mean number of glucose readings per day was 4.3 for preconception and 5.6 for third trimester. A1C was measured in EDTA-anticoagulated fresh blood samples, using a high-performance liquid chromatography DCCT (Diabetes Control and Complications Trial)-aligned method (Variant II HPLC analyzer; BioRad, Richmond, VA). The A1C reference intervals are 4–6%, and the interassay precision coefficient of variation for control materials with a DCCT-assigned A1C content of 5.3 and 9.6% is 2.1 and 2%, respectively. The A1C levels included in this study were the last measurement during preconception (nearest to conception) and the measurement nearest to 36 weeks' gestation.

Statistical analyses were conducted using SPSS version 8.0 statistical software (SPSS, Chicago, IL). To compare mean values among quantitative variables, the paired-samples Student's *t* test was used. Pearson correlation coefficient was used to measure the linear relation between A1C and mean glucose. Multivariate linear regression analysis was performed to estimate the effect of pregnancy on the relation between A1C and mean glucose. In this model, the dependent variable was A1C and the independent variables were mean glucose and pregnancy status. Pregnancy status was coded as a categorical variable (preconception = 0; third trimester = 1). Glucose and A1C are reported as means ± SD. A P value <0.05 was considered significant.

RESULTS

— Preconception mean glucose was 138.9 ± 17.9 mg/dl (range 88; median 140.5), and preconception A1C was 6.6 ± 0.6% (range 2.9; median 6.6), with a significant correlation between them ($r = 0.648$; $P < 0.001$). Third trimester mean glucose was 129.0 ± 13.1 mg/dl (range 48; median 129), and third trimester A1C was 6.0 ± 0.5% (range 2.2; median 6.1), with a significant correlation between them ($r = 0.580$; $P < 0.001$). There was a significant decrease both in mean glucose and in A1C ($P < 0.005$) from preconception to third trimester. The regression equation to predict A1C from mean glucose and pregnancy status was: A1C = 3.66 + (0.02 × mean glucose) + (−0.38 × pregnancy status). The R^2 of the model was 0.531 ($P < 0.001$). The SE for the constant was 0.33, and the SEs for the β-coefficients for mean glucose and pregnancy status were 0.02 and 0.08, respectively. Figure 1 shows the regression lines for the relation between A1C and mean glucose before pregnancy (pregnancy status = 0) and in late pregnancy (pregnancy status = 1).

CONCLUSIONS

— From our data, the regression line to predict third trimester A1C (pregnancy status = 1) would be: A1C = 3.66 + (0.02 × mean glucose) − 0.38, while the regression line to predict

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

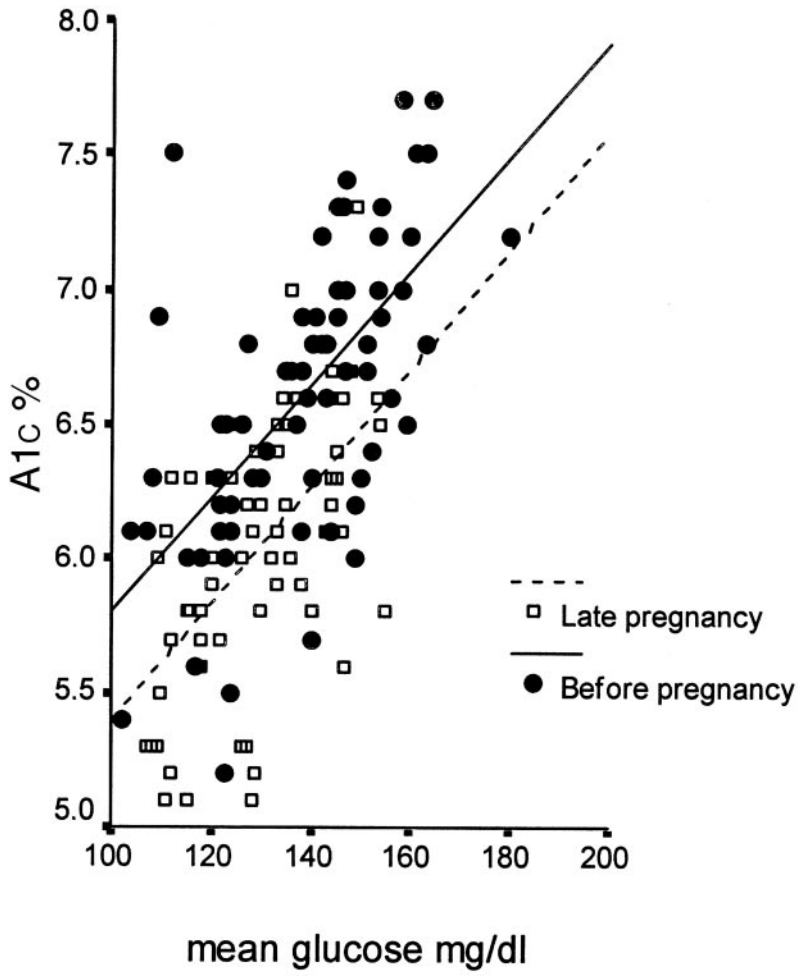

Figure 1—*Regression lines for the relation between A1C and mean glucose before pregnancy and in late pregnancy.*

preconception A1C (pregnancy status = 0) would be: A1C = 3.66 + (0.02 × mean glucose). This means that in women with type 1 diabetes, a reduction of ~0.4% in the A1C value can be expected in late pregnancy, which is not dependent on mean glucose levels. Figure 1 shows that for any mean glucose value, the A1C predicted will be lower in late pregnancy than before pregnancy (e.g., for a mean glucose of 140 mg/dl, the A1C would be 6.5% before pregnancy and 6.1% in late pregnancy).

Biological variation in A1C, which is distinct from that attributable to mean glucose, cannot account for the change observed. Variation of A1C between individuals, which represents the main source of A1C variation (11), does not influence our results, since the same women were studied before pregnancy and during pregnancy. Within-individual changes in A1C are too small (12) to explain a reduction of 0.4% in A1C.

Our results provide an additional explanation to the fact that near-normal A1C is insufficient for preventing diabetes-related complications of pregnancy (13,14), since the A1C value will be lower independently of glycemic control. While it seems difficult to achieve the glucose levels reported in healthy pregnant women (15), it is of clinical importance to note that when evaluating third trimester A1C levels in women with type 1 diabetes the value will be ~0.4% lower, without any improvement in glycemic control.

Several studies suggest that the normal upper reference range of A1C in pregnant women should be lower (1–3). Since in women with type 1 diabetes a decrease in third trimester A1C value will occur regardless of glycemic control, we conclude that the A1C goal in late pregnancy should be lowered 0.4% for pregnancies complicated with diabetes.

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