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Glycemic changes during menstrual cycles in women with type 1 diabetes☆

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ABSTRACT

Background and objective: To determine frequency of women with type 1 diabetes showing menstrual cyclic changes in glycemia, analyze their clinical characteristics, and assess the pattern of glycemic changes.
Patients and methods: We analyzed glucose meter readings along 168 menstrual cycles of 26 women with type 1 diabetes. We evaluated mean glucose, mean glucose standard deviation, mean fasting glucose, percentage of glucose readings >7.8 mmol/L and <3.1 mmol/L, and mean insulin dose in 4 periods for each cycle. A woman was identified as having cyclic changes when mean glucose rose from early follicular to late luteal in two-thirds of her menstrual cycles.
Results: A percentage of 65.4 of the women had cyclic changes. Characteristics of women with and without cyclic changes, including self-perception of glycemic changes, were similar with exception of age at diabetes diagnosis (22.5 [7.5] vs. 14.4 [9.5] years; $p = 0.039$). In women with cyclic changes mean percentage of glucose readings >7.8 mmol/L rose from early follicular (52.2 [16.3] %) to early and late luteal (58.4 [16.0] %, $p = 0.0269$; 61.0 [16.9] %, $p = 0.000$).
Conclusion: Almost two-thirds of women with type 1 diabetes experience a menstrual cycle phenomenon, attributable to an increase in hyperglycemic excursions during the luteal phase. Enabling women to evaluate their weekly mean glucose from their meter and exploring the causes of hyperglycemic excursions during luteal phase should ensure more accuracy when giving instructions for diabetes management in women with premenstrual hyperglycemia.

Cambios glucémicos durante el ciclo menstrual en mujeres con diabetes mellitus tipo 1

Palabras clave:
Ciclo menstrual
Cambios glucémicos
Diabetes tipo 1

RESUMEN

Fundamento y objetivo: Determinar la frecuencia de mujeres con diabetes tipo 1 que experimentan cambios glucémicos durante el ciclo menstrual, analizar sus características clínicas, y evaluar el patrón de los cambios glucémicos.
Pacientes y métodos: Analizamos las lecturas de los glucómetros a lo largo de 168 ciclos menstruales en 26 mujeres con diabetes tipo 1. Evaluamos la glucemia media, la desviación estándar media, la glucemia media basal, el porcentaje de lecturas > 7,8 mmol/l y < 3,1 mmol/l, y la dosis de insulina media en 4 períodos de cada ciclo. Se consideró que una mujer tenía cambios cíclicos cuando la glucemia media se elevó entre la fase folicular temprana y la fase lútea tardía en dos tercios de sus ciclos menstruales.
Resultados: El 65,4% de las mujeres experimentaron cambios cíclicos. Las características de las mujeres con y sin cambios cíclicos, incluyendo la autopercepción de cambios glucémicos, fueron similares, exceptuando la edad de diagnóstico de la diabetes (22,5 [7,5] frente a 14,4 [9,5] años; p = 0,039). En mujeres con cambios cíclicos el porcentaje medio de los valores de glucosa > 7,8 mmol/l se elevó entre la fase folicular temprana (52,2 [16,3] %) y la fase lútea temprana y tardía (58,4 [16,0] %, p = 0,0269; 61,0 [16,9] %, p = 0,000).

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Conclusión: Casi dos tercios de las mujeres con diabetes tipo 1 experimentan fenómenos del ciclo menstrual atribuibles a un incremento de las excursiones hiperglucémicas durante la fase lútea. Posibilitar que las mujeres evalúen su glucemia media semanal a partir de las lecturas de los glucómetros, y explorar las causas de las excursiones hiperglucémicas durante la fase lútea podría garantizar una mayor precisión al impartir instrucciones para la gestión de la diabetes en mujeres con hiperglucemia premenstrual.

Introduction

It is not unusual for diabetes practitioners to come across the comment from women with type 1 diabetes that their fluctuations in blood glucose control are the effect of the menstrual cycle. It is generally agreed that perimenstrual changes in blood glucose occur in some, but not all women with type 1 diabetes,[1] with the percentage of women experiencing a menstrual cycle phenomenon varying from 44% to 61%.[2–5] However, studies addressing this issue are of limited value, since the number of women included in the studies is low[2,4,5] or the results are based on self-reported changes.[3]

The most common pattern in the menstrual cycle phenomenon is an increase in blood glucose during the luteal phase,[2–6] which has been attributed to changes in insulin sensitivity along the menstrual cycle,[2,4,7] though some studies have not found variations in insulin sensitivity related to the menstrual cycle.[8,9] The presence of premenstrual syndrome[10,11] or changes in appetite, energy intake or gastric emptying[10,12] may account for the premenstrual hyperglycemia.

The general recommendation given to adjust insulin requirements during the premenstrual period is to increase overnight insulin dose[13] or overall basal insulin rate.[14]

To ensure more accuracy when giving instructions for diabetes management to women in their reproductive years this study aimed to determine the percentage of women with type 1 diabetes who experience cyclic changes in glycemia, to analyze which clinical characteristics relate to the menstrual cycle phenomenon, and to evaluate the changes in glycemic parameters along the menstrual cycle.

Subjects, materials 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. We retrospectively analyzed 168 menstrual cycles from 26 women with type 1 diabetes who were on preconceptional care (mean number of menstrual cycles per women: 6.5 (2.2)) during two consecutive years. Only women with complete glucose data were included. The participants had a mean age of 35 (5.4) years, a mean diabetes duration of 15.3 (6.3) years and a mean BMI of 22.7 (2.3) kg/m^2. Four women had diabetic retinopathy and one woman had diabetic nephropathy. None of the women used hormonal contraception during the study. Eleven women had already had a child and 17 had a child after the study period, and none required treatment for infertility. Mean age at menarche was 12.5 (6.3) and in 23 subjects menarche had occurred before the diagnosis of diabetes. Only regular menstrual cycles were included in the study (cycle length 21–35 days)[15] and, if pregnancy ensued, the last menstrual cycle before conception was not included in the study.

All women were on insulin pump therapy and were instructed on insulin dose adjustment, correcting doses and carbohydrate counting. Total daily insulin dose was downloaded to a computer from insulin pumps. Women performed home blood glucose monitoring (6.6 (0.9) glucose readings/day) using the One Touch UltraSmart (LifeScan, Milipitas, CA). The glucose readings stored in the meter were downloaded to a computer.

A1c was measured in each subject at the end of the study period using high performance liquid chromatography DCCT (Diabetes Control and Complications Trial)-aligned method (Variant II HPLC analyzer; BioRad, Richmond, VA). The A1C reference intervals are 20–42 mmol/mol (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.

For each menstrual cycle we evaluated mean glucose, mean glucose standard deviation, mean fasting glucose, percentage of glucose readings above 140 mg/dl (7.8 mmol/L), percentage of glucose readings below 55 mg/dl (3.1 mmol/L) and mean insulin dose in four consecutive periods: early follicular phase (mean length 7.2 ± 1.4 days), late follicular phase (mean length 7.5 ± 1.6 days), early luteal phase (7 days) and late luteal phase (7 days). To determine the day of ovulation we subtracted 14 days from the length of a complete menstrual cycle.[4] To calculate early follicular and late follicular phase the total days of the follicular phase were divided by two.

A woman was identified as having cyclic changes in glycemia when mean glucose rose (at least 15 mg/dl) from early follicular phase to late luteal phase in two thirds of her menstrual cycles. At the end of the study period all, but one woman, were interviewed for symptoms of premenstrual syndrome and self-perception of premenstrual changes in glycemic control. The telephone inquiry included three items: (1) ¿Do you have premenstrual symptoms? (2) ¿Do you experience perimenstrual changes in glucose levels? And if yes: (3) ¿what type of glycemic changes do you observe?

Statistical analyses were conducted using SPSS version 11.0 statistical software (SPSS, Chicago, IL). To compare mean values among quantitative variables, the independent-samples Student's *t*-test or, when appropriate, the Mann–Whitney *U* test were used. For multiple comparisons the one way analysis of variance, with the Bonferroni procedure for post hoc contrasts, was used. To compare categorical variables, the chi-square test and the Fisher exact test were used. Data are reported as means ± SD or as percentage. A p value (bilateral) <0.05 was considered significant.

Results

Of the 26 women, 17 (65.4%) had cyclic changes in glycemia related to the menstrual cycle. Fig. 1 is an example of the pattern of glucose in a woman with cyclic changes and in a woman without cyclic changes. Characteristics of women with cyclic changes in glycemia and those without cyclic changes in glycemia were similar, with the exception of age at the diagnosis of diabetes (Table 1).

A1c at the end of the study period was not significantly different in women with and without cyclic changes in glycemia: 50 (7) vs. 48 (10) mmol/mol; (6.7 (0.6) vs. 6.5 (0.9) %); $p = 0.075$.

Mean glucose during the early follicular phase was similar in women with and with out cyclic changes in glycemia (7.6 (1.6) vs. 7.3 (1.5) mmol/L; $p = 0.290$). In women with cyclic changes in glycemia mean glucose rose significantly from early follicular to luteal phase (early luteal: 8.2 (1.5) mmol/L; $p = 0.041$ and late luteal: 8.4 (1.7) mmol/L; $p = 0.000$). In women without cyclic changes