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Sedentary behavior in obese pregnant women is associated with inflammatory markers and lipid profile but not with glucose metabolism

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ABSTRACT

Background: Sedentary behavior is an independent risk factor for the metabolic syndrome, but the role of sedentary behavior in the development of gestational diabetes is unclear.
Objectives: This study tested the hypothesis that less sedentary behavior is related to better insulin sensitivity, lipid and cytokine profile in obese pregnant women.
Methods: A longitudinal observational study with 46 overweight and obese pregnant women was conducted. Sedentary behavior was measured objectively using accelerometers at 15, 24 and 32 weeks of gestation, and at those time points fasting blood was taken as well. A 100 g oral glucose tolerance test was performed at 24 and 32 weeks. Levels of glucose, insulin, total cholesterol, HDL, LDL, triglycerides were measured, as well as cytokines. The relationship between sedentary behavior and metabolic outcomes was assessed using linear regression analysis.
Results: Women spent almost 60% of their time sitting throughout pregnancy. In cross-sectional analyses, an association of sedentary time at 24 weeks was found with increased total cholesterol and HDL. More sedentary time was associated with lower IL-6 at 24 weeks and with higher IL-10, TNF-α and leptin levels at 32 weeks of pregnancy. Changes in sedentary time were not associated with changes in any of the metabolic outcomes.
Conclusions: In conclusion, time spent sedentary in pregnancy was associated with lipid and cytokine profile. Whether decreasing sedentary time beneficially influences lipid profile and influences cytokine profiles of overweight and obese women needs to be assessed in future intervention studies.

1. Introduction

Physical activity before and in early pregnancy is associated with a lower risk of developing gestational diabetes (GDM) [1]. Physical activity increases both insulin-mediated and non-insulin mediated glucose disposal. Physical activity is also known for improving glucose homeostasis through its direct or indirect impact on insulin sensitivity via several other mechanisms such as lipid metabolism [2]. Previously, we reported an association of moderate-to-vigorous physical activity (MVPA) with first phase insulin response and insulin sensitivity in pregnancy [3], which might be mediated by interleukin (IL)-6 [4]. However, during pregnancy most women decrease their daily physical activities and participate less in exercise and sports [5].

Evidence is accumulating that, independent of physical activity, sedentary behavior is related to increased mortality and morbidity [6,7]. Sedentary behavior is defined as being engaged in activities at the level of resting energy expenditure which includes activities such as sitting, lying down, computer activities and watching television [8]. Sedentary behavior is an important independent risk factor for the development of insulin resistant conditions, such as the metabolic syndrome [9,10] and type 2 diabetes [11]. The role of sedentary behavior for insulin resistance in pregnancy and the development of GDM is not well understood, since most previous studies focused on physical activity only.

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We hypothesized that obese and overweight women spending less hours in sedentary behavior have lower fasting glucose and insulin levels, higher insulin sensitivity, have a healthier lipid profile, and a less pro-inflammatory cytokine profile. Cytokines of interest were those that reflect inflammatory status (CRP, IL-6, IL-10, TNF-α, IL-1β) and/or are related to insulin sensitivity (IL-6, leptin, adiponectin) [4,12–17]. To test these hypotheses, we determined the cross-sectional and longitudinal relationships between objectively measured sedentary behavior and estimates of fasting blood glucose, fasting insulin, insulin sensitivity, first and second phase insulin response, lipids and cytokines.

2. Research design and methods

2.1. Study design

This longitudinal study was conducted between January 2007 and January 2011. Approval of the Medical Ethics Committee of VU University Medical Centre in Amsterdam (2007/133) was obtained.

2.2. Subjects

Participants were overweight (Body Mass Index (BMI) $\geqslant$ 25) and obese (BMI $\geqslant$ 30) pregnant women, who are at increased risk for gestational diabetes mellitus (GDM). These pregnant women were selected based on their pre-pregnancy BMI. Other additional inclusion criteria were gestational age <15 weeks, age $\geqslant$18, no diabetes mellitus or history of GDM, and adequate knowledge of Dutch language. Pregnant women were excluded from the study if they were diagnosed with GDM at baseline, were using medication that affects insulin secretion or insulin sensitivity, or if they had any chronic medical conditions or psychiatric problems. All women provided written informed consent. The study sample consisted of 46 women for whom data were available from accelerometers and fasting blood samples collected at three time points.

2.3. Sedentary behavior and physical activity measurement

Sedentary behavior was measured by an accelerometer (Actigraph GT3X+, GT1M or Actitrainer) worn for four days by the pregnant women on the right hip at all times except at night during sleep and during water-based activities. The accelerometers collected data in 1-min epochs and the unit of data was counts per minute. For valid data, the accelerometer had to be worn at least 8 h per day, which was calculated after periods of consecutive zero counts $\geqslant$30 min were removed. Participants had to wear the accelerometer for a minimum of 3 days to be included in the analyses.

Sedentary time was calculated in minutes per day, using the Freedson cut-off point of <100 counts/min [18]. Sedentary behavior was calculated as a percentage of total wear time, by dividing the time spent sedentary by the total wear time of that day. Sedentary time as percentage of total wear time was averaged over the days the accelerometer was worn.

In addition time spent in moderate-to-vigorous physical activity (MVPA) [>1952 counts/min] was calculated. For MVPA, the average hours per week were calculated by adding up the total time in MVPA in hours, dividing this by the number of days the accelerometer was worn and then multiplying by seven.

2.4. Blood samples

Venous blood samples were collected at 15, 24 and 32 weeks of gestation after 10 h of overnight fasting. An oral glucose tolerance test (OGTT) was conducted at 24 and 32 weeks of gestation. For the OGTT, after the collection of blood for fasting tests, women were given a glucose drink (100 g glucose in 500 ml of water) and blood samples were collected at 30, 60, 90, 120 and 180 min. Women were not allowed to eat during the test. Women with a threshold plasma glucose concentration above 5.3 mmol/l (fasting), or 10.0 mmol/l (60 min), or 8.6 mmol/l (120 min) or 7.8 mmol/l (180 min) were diagnosed as GDM [19].

Glucose (mmol/l), insulin (pmol/l), total cholesterol (mmol/l), HDL-cholesterol (HDL-C; mmol/l), LDL-cholesterol (LDL-C; mmol/l) and triglycerides (mmol/l) were measured as described below.

2.5. Biochemical analyses

Plasma glucose was measured by a Glucose/HK kit (Glucoquant; Roche/Hitachi Modular P analyzer; Roche Diagnostics GmbH, Mannheim, Germany) and insulin by immunometric assay (Luminescence, Advia Centaur, Siemens Medical Solutions Diagnostics). Total cholesterol, triglycerides, and HDL-C were measured with commercial enzymatic kits on Roche/Hitachi modular P analyzers (Roche Diagnostics GmbH, Mannheim, Germany), whereas LDL-C was calculated using the Friedewald formula [20]. Insulin sensitivity was estimated with the HOMA index [21]. Using Stumvoll equations: $1194 + 4.724 * \text{Ins0} - 117.0 * \text{Glu60} + 1.414 * \text{Ins60}$ and $295 + 0.349 * \text{Ins60} - 25.72 * \text{Glu60} + 1.107 * \text{Ins0}$, first phase insulin response and second phase insulin response was estimated respectively [22].

Protein levels of cytokines (CRP, IL-6, IL-10, TNF-α, IL-1β, leptin, and adiponectin) in the serum samples were quantified by multiplex assay according to manufacturer's instructions (eBioscience, San Diego, CA, USA).

2.6. Covariates

Information on age, pre-pregnancy body weight and height, ethnicity (White European/non-white (mostly from Morocco and Surinam), level of education (low = 10 years of education or less, middle = 11–14 years of education, high = 15 years of education or more), history of type-II diabetes in first line relatives as well as employment status were recorded. Maternal body weight was measured at 15, 24 and 32 weeks using calibrated electronic scales, with participants wearing only indoor clothing and no shoes. Prepregnancy weight was self-reported. At the first measurement, maternal body height was measured with bare feet and a (wall-mounted) height scale. Body Mass Index (BMI, kg/m^2) was calculated based on self-reported prepregnancy weight, and measured weight at 15, 24 and 32 weeks.

2.7. Statistical analysis

Values of continuous variables are expressed as mean with standard deviation for normally distributed variables, and as median and interquartile range (IQR) for skewed variables. In the figures, box-plots with whiskers indicating the 10–90th percentiles are presented. To test for differences in sedentary behavior, cytokines and insulin parameters over time, paired Wilcoxon Rank tests were used. Changes in sedentary time and in metabolic outcomes were calculated as the value at 24 or 32 weeks minus the value at 15 weeks.

To test for differences in metabolic outcomes between tertiles of percentage of sedentary time, *T*-tests (normally distributed data) or Kruskal-Wallis tests (skewed data) were used. The cross-sectional relationship between the percentage of wearing time spent in sedentary habits at all three time points and metabolic outcomes at the same time points were assessed using linear regression analysis. For these models, a natural log-transformation was performed on cytokine data. Results of regression analyses are presented as beta-values and 95% confidence interval (CI).