

Low activity in pregnancy does not modify neither adiponectin nor leptin serum levels

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Aim. Obesity in pregnancy is increasing and is a risk factor for metabolic pathology and is associated with dyslipidemia, vascular dysfunction, and low-grade chronic inflammation. Our aim was to measure adiponectin and leptin in lean and overweight-obese pregnant women in the first and second halves of pregnancy and its relation to walked distance as measured with pedometers.

Methods. Forty-two women in the first trimester of pregnancy were recruited, 21 with a pregestational body mass index (BMI) <25 kg/m² and 21 with a BMI ≥25 kg/m² matched for parity. Serum levels of adiponectin and leptin were measured by ELISA technique. Daily step count was measured with pedometer (Sportline 330, USA).

Results. In the first half of pregnancy there were statistically significant differences in age ($p \leq 0.05$), weight ($p \leq 0.001$), BMI ($p \leq 0.001$), leptin ($p \leq 0.001$) and adiponectin/leptin ratio ($p \leq 0.05$). In the first half of pregnancy, although the overweight-obesity group walked an average of one km more than the normal weight group, its leptin values doubled that of the second group, which showed a tendency in adiponectin to be higher. In the second half of pregnancy the walked distance was equal in both groups. Likewise, adiponectin values decreased in both groups, but the decrement was much greater in the overweight-obesity group. On the other hand, leptin values increased in both groups and, although the tendency was to be higher in the overweight-obesity group, the statistical difference was lost. Av-

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erage weekly energy expenditure in our patients was light (1.5-2.9 METs). Low activity way of living during pregnancy doesn't seem to alter adiponectin serum levels beyond the influence of BMI. In our study, leptin serum levels were determined in the first half of pregnancy by the BMI and not by the physical activity.

Conclusion. Neither adiponectin nor leptin are modified by low activity in Mexican pregnant women as measured with pedometers.

KEY WORDS: Adiponectin - Body Mass Index - Leptin - Obesity - Pregnancy.

Physical activity during pregnancy is a desired mean to low the incidence of weight-gain complications. Regarding perinatal outcomes, mild to moderate exercise is safe for pregnant women with overweight and obesity.¹ Current American College of Obstetricians and Gynecologists

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cologists (ACOG) guidelines recommend engaging in 30 min of moderate-intensity physical activity during most days of the week for pregnant women without medical or obstetrical complications² and are consistent with guidelines for non-pregnant women.³ The guidelines, which emphasize the accumulation of physical activity through bouts of at least 10 min, may be more acceptable to pregnant women than traditional exercise recommendations.⁴ However, the majority of pregnant women currently do not meet physical activity guidelines, with rates of compliance ranging from 13–20%.^{5–8}

Walking is the primary mode of recreational activity for many pregnant women.⁹ Initiating a mild walking program during pregnancy, combined with nutritional control may promote healthy lifestyle changes especially with overweight and obese women. Previous studies support the use of pedometers as a motivational tool and have observed a significant impact on walking behavior,¹⁰ but few studies have confirmed the positive effect of exercise in modulating the adipokine expression. The purpose of this study was to register the mean daily steps in Mexican pregnant women with or without overweight-obesity and to determine their association with the serum expression of adiponectin and leptin.

Materials and methods

Type of study and setting

This was a non-randomized, prospective, comparative and longitudinal study conducted at the Materno Perinatal Hospital "Mónica Pretelini" (HMPMP), Toluca, Mexico, in the period January 1st 2010 to November 30, 2011.

Data

The data accessed in the clinical record of each patient were entered in an Excel spreadsheet previously designed by the researchers.

Sample size

Accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, with a common standard deviation of 5.12 and a drop-out rate of 20%, 21 pregnant women per group are necessary to recognize as statistically significant difference greater than or equal to 5 ng/ml in leptin serum level.

Subjects

Women who had received medical attention for her pregnancy at the HMPMP. We excluded women with hypertension, collagen vascular diseases, inflammatory bowel disease and chronic inflammatory conditions, or if they were using corticosteroids. Women with incomplete medical records were removed from the study.

Recruitment

Women were recruited at their first visit at 10–12 wk gestation. They were asked to attend after an overnight fast and underwent testing between 0700 and 0900 h. Two groups of pregnant women were conformed: a) with pregestational normal weight (body mass index (BMI) <25 kg/m²) and b) with pregestational overweight-obesity (BMI ≥25 kg/m²). The diagnosis of Gestational Diabetes Mellitus was made according to the National Diabetes Data Group (NDDG).¹¹

Clinical follow-up

Two complete examinations were performed in the first and second half of pregnancy. On the morning of each examination body weight was rounded to the nearest 0.1 kg (Seca 700, Germany). Blood pressure was recorded at each visit using a standard sphygmomanometer (Riester Big Ben® Square, Germany) and appropriately sized cuff.

Diet

All women were given individualized dietary advice from a qualified nutritionist.

Compliance with the dietary regimen was evaluated monthly.

Physical activity

Participants were provided with a digital pedometer (Sportline 330, USA) to encourage self-monitoring. Ten women were previously evaluated to calculate the distance in their steps to get a media of the Mexican population. Daily steps for "sedentary" individuals were <5000, 5000–9999 daily steps were classified as "low active" and $\geq 10,000$ steps were the "active" category.¹² An average was determined with all the values of the days of the previous month before the date of the medical consultation.

Laboratory

During each consult, with a fasting period of eight hours we measured glucose (mg/dL), cholesterol (mg/dL), high-density lipoproteins (HDL) (mg/dL), low-density lipoproteins (LDL) (mg/dL) and triglycerides (mg/dL) (Dimensión Rx I Max, Dade Behring). Very-low-density lipoproteins (VLDL) were calculated as triglycerides (mg/dL)/5.

Adipokines

Adiponectin and leptin serum concentrations were measured using an enzyme-linked immunosorbent assay (ELISA) according to manufacturer's instructions (GenWay Biotech, Inc, High sensibility ELISA Sandwich Adiponectin reference 40-055-200002 and Human Leptin ELISA Sandwich reference 40-055-200004 respectively).

Statistical analysis

We used the SPSS version 16. Continuous variables were expressed in media (range). We used Kruskal Wallis and Mann-Whitney U test. A p value ≤ 0.05 was considered statistically significant.

Ethical concerns

This study was approved by the Ethical and Research Committee of the HMPMP and informed consent was obtained from every participant at the beginning of the study.

Results

Subjects

We followed 21 women of normal weight age 21 (15–35) and 21 women who were overweight-obese age 28 (15–43). Table I shows the clinical and laboratory characteristics of the studied population.

Measures

STEP COUNT

The average distance per step of Mexican pregnant women was of 0.52 m. According to the daily steps in the first half of pregnancy only three women in the normal weight group were classified as active. Of these, two were still active in the second half of pregnancy, one decreased to be low active and one low active woman in the first half of pregnancy became active in the second one. In the group of overweight-obesity, only one woman was active in the first half of pregnancy while in the second one this same woman was low active and three low active women became active. We did not find a significant Spearman correlation neither between km walked and adiponectin nor between km walked and leptin.

ANTHROPOMETRIC AND LABORATORY DATA

In the first half of pregnancy there were statistically significant differences in age ($p \leq 0.05$), weight ($p \leq 0.001$), BMI ($p \leq 0.001$), leptin ($p \leq 0.001$) and adiponectin/leptin ratio ($p \leq 0.05$). In this period of time, although the overweight-obesity group walked an average of one km more than the normal weight group, its leptin values doubled that

TABLE I.—Sociodemographic and clinical characteristics.¹

Variable	BMI	
	< 25 (n = 21)	≥ 25 (n = 21)
Age (years) ^a	21 (15-35)	28 (15-43)
Pregnancies	2 (1-3)	2 (1-5)
Pregestational weight (kg) ^{***}	53.5 (42-60)	64 (57-95)
PGBMI (kg/m ²) ^{***}	22 (16.8-24.6)	26.8 (25.6-40)
Glucose (mg/dL) ^a	79.5 (70-102)	86.5 (72-150)
BMI (kg/m ²) ^{b***}	22.5 (18.4-24.9)	27.6 (25.4-36.8)
Glucose (mg/dL) ^b	74.5 (72-89)	79 (66-89)
Cholesterol (mg/dL) ^a	157 (69-236)	169 (134-240)
Cholesterol (mg/dL) ^b	219 (186-271)	204 (61-295)
Triglycerides (mg/dL) ^a	123 (56-297)	118 (47-208)
Triglycerides (mg/dL) ^b	235 (192-427)	221 (125-326)
HDL (mg/dL) ^a	62 (44-123)	51 (36-73)
HDL (mg/dL) ^b	63 (49-102)	56 (38-188)
LDL (mg/dL) ^a	97 (54-159)	92 (62-151)
LDL (mg/dL) ^b	122.5 (62-159)	124 (91-152)
VLDL (mg/dL) ^a	24.6 (11.2-59.4)	23.6 (9.4-41.6)
VLDL (mg/dL) ^b	47 (38.4-85.4)	44.2 (25-65.2)
Adiponectin (µg/dL) ^a	88.5 (51.9-135.8)	84.5 (44.7-120.2)
Adiponectin (µg/dL) ^b	77.9 (36-111.6)	76.2 (36-89.2)
Leptin (ng/dL) ^{***}	9.6 (2.3-13.3)	18.3 (11-24.9)
Leptin (ng/dL) ^b	19.1 (7.1-34.3)	20.3 (14.1-31.5)
Adiponectin/leptin ratio ^{a*}	12 (4.1-46.2)	4.7 (3.1-7.1)
Adiponectin/leptin ratio ^b	4.2 (1-13.1)	3.2 (2.1-4.7)

¹ media (range); HDL: high-density lipoproteins; LDL: Low-density lipoproteins; VLDL: very low-density lipoproteins; BMI: body mass index; PGBMI: pregestational body mass index; a: first half of pregnancy; b: second half of pregnancy. * $p < 0.05$; *** $p < 0.001$.

of the second group, which showed a tendency in adiponectin to be higher.

In the second half of pregnancy the walked distance was equal in both groups but the difference in BMI was kept ($p \leq 0.001$). Likewise, adiponectin values decreased in both groups, but the decrement was much greater in the overweight-obesity group. On the other hand, leptin values increased in both groups and, although the tendency was to be higher in the overweight-obesity group, the statistical difference was lost as occurred with the adiponectin/leptin ratio.

In addition to the previous analysis, comparing the results of women who were normal weight with women who were overweight-obese discarding those who were diabetic ($n = 4$), there were statistically significant differences in weight ($p \leq 0.001$), BMI ($p \leq 0.001$), HDL ($p \leq 0.05$) and leptin ($p \leq 0.01$) in the first half of pregnancy. In this same period, whereas both groups had almost the same values of adiponectin, leptin values were more than double in the

group of overweight-obesity despite having walked a longer distance per day than the normal weight group. Furthermore, in the second half of pregnancy adiponectin values decreased in both groups, but this reduction was even more in the overweight-obesity group which also walked less km. Conversely, leptin values increased in both groups but remained higher in the overweight-obesity group.

We also noted that, if comparing women of overweight-obesity versus women with diabetes, there were statistically significant differences in age ($p \leq 0.01$) and height ($p \leq 0.05$) at the beginning of the study, but not in adiponectin and leptin.

Discussion

Interventions to reduce gestational weight gain are important modifiable risk factors for maternal and fetal perinatal complications.¹³ In this regard there are studies

with two principal approaches, those where intervention is based only on education regarding diet and exercise¹⁴⁻¹⁷ and those with supervised exercise.¹⁸⁻²⁰ In both cases, when controlled, walking has been effective prevention of excessive weight gain during pregnancy,^{17, 18, 21, 22} combined with nutritional management.

The exercise of mild to moderate intensity is recommended to any pregnant woman even those who wish to start an active life during pregnancy. In this case, it is recommended to gradually increase the time and intensity of exercise.² Moreover, the execution of a regular program of exercise provides benefits for healthy living the gestational period, reducing the incidence undesirable effects during pregnancy,^{23, 24} in addition to improving cardiovascular function.²⁵

Pregnant women often have low total physical activity levels²⁶ and these tend to reduce further in the later stages of pregnancy.²⁷ Unfortunately, it is difficult to motivate former sedentary women to fulfill the ACOG exercise recommendations.² Our results support this conclusion, since the 2000 Compendium of Physical Activities gives a metabolic equivalent (MET) of 2 for walking less than 2.0 mph, level ground (code 7151),²⁸ average weekly energy expenditure in our patients was light (1.5-2.9 MET's).

In relation to obesity in pregnancy the ACOG takes no position on the safety of the exercise, but several studies have showed no significant difference between women who practiced physical exercise and the control group and the perinatal outcomes,^{14, 16, 18, 19, 29} only morbid obesity appears as a relative contraindication of this practice. In our cohort 16 women were overweight, two had grade I obesity and two grade II obesity, we only had one morbidly obese woman.

Reduced cord concentrations of growth-related peptides has been associated with regular exercise, suggesting an influence of physical activity on endocrine regulation of fetal growth.³⁰ In this regard, maternal hormonal alterations in response to exercise training may be associated with the regulation of nutrient availability.

The literature regarding the effect of exercise on adiponectin is controversial. For example, exercise's stimulatory effect on adiponectin gene expression has been published previously.³¹ In contrast, it has also been published a lack of effect of exercise on circulating adiponectin.³² These disparities may be influenced by fat metabolism.³³

Taken in the context of other work,³⁴ in our cohort there was also a reduction in adiponectin levels during the second half of pregnancy. It is clear from this study that low activity way of living during pregnancy does not seem to alter adiponectin serum levels beyond the influence of BMI.

Exercise, with concomitant changes in systemic hormone levels and energy expenditure, may contribute to the regulation of plasma leptin levels and presumably, leptin action. The most compelling evidence to date of the interaction between exercise, energy balance and systemic leptin in humans has underscore the importance of clearly defining the balance between energy intake and energy expenditure when studying the physiology of leptin.³⁵

Generally speaking, leptin decreases in pregnancy if women practice regular exercise.³⁶ Should the leptin serum levels decrease in exercising pregnant women, this may reflect subtle changes within the placenta.³⁷ In our study, leptin serum levels were determined in the first half of pregnancy by the BMI and not by the physical activity.

This study further establishes a role for the adiponectin/leptin ratio when analyzing the effect of physical activity on pregnancy. For instance, this ratio was statistically significant in the first half of pregnancy but with lower p than leptin alone, suggesting that low physical activity is not enough to produce differences in adipokine expression and metabolism.

We recognized that there are limitations to our study design. This was not a randomized controlled trial. Other limitations include self-reported pre-pregnancy height and body mass, which tend to be slightly different from when directly measured;

however, these approaches have been used in the literature.³⁸

We conclude that low activity in pregnancy doesn't modify neither adiponectin nor leptin serum levels but it is necessary to take into account several variables when analyzing adipokine changes with the level of physical activity during the gestational period. We'll leave to future cohorts the question of whether moderate exercise does modify the adipokine expression irrespective of BMI.

Riassunto

La scarsa attività in gravidanza non modifica né i livelli sierici di adiponectina né di leptina

Obiettivo. L'obesità in gravidanza è in aumento, è un fattore di rischio per la patologia metabolica ed è associata a dislipidemia, disfunzione vascolare e infiammazione cronica di basso grado. Il nostro obiettivo era quello di misurare adiponectina e leptina nelle donne gravide magre e sovrappeso-obese nella prima e nella seconda metà della gravidanza e il relativo rapporto alla distanza di camminata misurata con pedometro.

Metodi. Sono state arruolate quarantadue donne nel primo trimestre di gravidanza, 21 con un indice di massa corporea pre-gestazionale (BMI) <25 kg/m² e 21 con un BMI ≥ 25 kg/m² abbinata per parità. I livelli sierici di adiponectina e leptina sono stati misurati mediante tecnica ELISA. Il conteggio giornaliero dei passi è stato misurato con pedometro (Sportline 530, USA).

Risultati. Nella prima metà della gravidanza si sono manifestate differenze statisticamente significative di età (p<0,05), peso (p<0,001), BMI (p<0,001), leptina (p<0,001) e rapporto di adiponectina/leptina (p<0,05). Nella prima metà della gravidanza, sebbene il gruppo sovrappeso-obesità percorresse una media di un km in più rispetto al gruppo di peso normale, i valori della leptina raddoppiavano quelli del secondo gruppo, che mostrava una tendenza ad una maggiore adiponectina. Nella seconda metà della gravidanza la distanza percorsa era uguale in entrambi i gruppi. Analogamente, i valori dell'adiponectina sono diminuiti in entrambi i gruppi, ma il decremento era maggiore nel gruppo di sovrappeso-obesità. D'altra parte, i valori della leptina sono aumentati in entrambi i gruppi e, sebbene la tendenza fosse superiore nel gruppo sovrappeso-obesità, la differenza statistica si perdeva. Il dispendio energetico medio settimanale delle pazienti era leggero (1,5-2,9 MET). Il tipo di vita con una scarsa attività durante la gravidanza non sembra alterare i livelli sierici di adiponectina

oltre l'influenza del BMI. Nel nostro studio, i livelli sierici di leptina sono stati determinati nella prima metà della gravidanza dal BMI e non dall'attività fisica.

Conclusioni. Né adiponectina né leptina vengono modificate da una scarsa attività nelle donne gravide messicane secondo quanto misurato con pedometro.

PAROLE CHIAVE: Adiponectina - Indice di massa corporea - Leptina - Obesità - Gravidanza.

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