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Maternal physiological changes at rest induced by exercise during pregnancy: A randomized controlled trial

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ABSTRACT

Objective: to analyse maternal physiological changes in several areas (cardiovascular, metabolic, renal and hepatic) related to the regular practice of a supervised exercise program.
Methods: This is an unplanned secondary analysis from a randomized controlled trial carried out in a single maternity unit in Madrid, Spain (NCT 02,756,143). From November 2014 to June 2015, 92 women were randomly assigned to perform a mild-moderate supervised exercise program during pregnancy (Intervention group, IG) or to continue with their routine pregnancy care (control group, CG). For the purpose of this study we collected clinical and analytical data (heart blood pressure, weight, blood glucose, AST, ALT, blood Creatinine and blood Uric acid) available from all obstetric visits and examined the differences between groups.
Results: We did not find any differences in: pregnancy weight (IG: 11.4 ± 4.4 Kg vs. CG: 10.1 ± 5.3 Kg; $p = 0.173$); fasting glucose at 10^{+0}–12^{+6} weeks (IG: 78.48 ± 8.34 vs. CG: 76 ± 13.26, $p = 0.305$) or at 34^{+0}–36^{+4} weeks (IG: 73.25 ± 10.27 vs CG: 73.45 ± 8.29,$p = 0.920$), and 50 gs glucose tolerance at 24^{+4}–26^{+6}weeks (IG: 116.23 ± 35.07 vs CG: 116.36 ± 25.98, $p = 0.984$); Aspartate-amino-transferase at 10^{+0}–12^{+6} weeks (IG: 15.38 ± 4.17 vs CG: 17.33 ± 7.05, $p = 0.124$) and at 34^{+0}–36^{+4} weeks (IG: 21.65 ± 5.25 vs CG: 19.53 ± 8.32, $p = 0.165$) or Alanine-amino- transferase at 10^{+0}–12^{+6} weeks (IG: 27.50 ± 10.63 vs CG: 28.27 ± 11.77, $p = 0.746$) or at 34^{+0}–36^{+4} weeks (IG: 22.93 ± 9.23 vs CG: 20.84 ± 13.49, $p = 0.407$); blood Creatinine concentrations at 34^{+0}–36^{+4} weeks (IG: 0.595 ± 0.401 vs CG: 0.575 ± 0.100, $p = 0.757$) and blood uric acid concentrations at 34^{+0}–36^{+4} weeks (IG: 3.526 ± 0.787 vs CG: 3.262 ± 0.672, $p = 0.218$). Heart blood pressure was similar between groups except at 27^{+0}–28^{+6} weeks, where systolic blood pressure was significantly lower in the CG in comparison to the IG (116.31 ± 10.8 mmHg vs. 120.22 ± 10.3 mmHg, $p = 0.010$).
Conclusion: Regular supervised exercise during pregnancy does not alter normal maternal physiology.

1. Introduction

Regular exercise mediates several physiological modifications in the human being, contributing to the prevention of several illnesses and to the personal wellbeing. In order to prevent obesity and several cardiovascular and metabolic illness, the World Health Organization (WHO) has published a guideline proposing the minimal activity recommended according to ages [1].

Cardiovascular changes at rest have been described in pregnant women that are under a supervised mild-moderate exercise program during pregnancy, like lower heart rate levels or lower heart blood systolic and diastolic pressures [2–5]. This would reflect a positive adaptation of the maternal cardiovascular system to the exercise and it may reduce the risk of preeclampsia during pregnancy [6].

Regarding metabolism, a good supply of nutrients is essential during pregnancy [7]. Exercise increases the use of glucose by the muscles, and it has been shown that a decrease in the blood glucose just occurs for a short period of time during prenatal exercise and, more acutely during the third trimester. Additionally, exercise during pregnancy elevates circulating triglyceride levels [8]. It has been reported that acute exercise in pregnant women, as opposed to choric exercise training, is associated with increased sympatho-adrenal and neurohumoral activity[7,9]. On the other hand, regular exercise, during pregnancy reduces glucose levels at the screening test for gestational diabetes (50 gs Glucose Tolerance Test) at 24–28 weeks of gestation [10]. At renal level, no effect has been concluded when performing moderate exercise during pregnancy [8].

Most studies conclude that the regular practice of mild to moderate exercise during pregnancy is not only safe but even positive for both, the mother and

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1 These author have equally contributed to this paper, and therefore both will have the first position on the author´s order.

the future new-born [4], although the underlying physiological changes are not well established.

The aim of the present study was to analyse physiological changes in the maternal cardiovascular, metabolic, renal and hepatic systems, in relation to the regular practice of a supervised mild-moderate exercise program. We hypothesized that this exercise during pregnancy would not alter the normal maternal physiology.

2. Methods

2.1. Trial design and participants

This is an unplanned secondary analysis of a randomized controlled trial (RCT), performed at the Hospital Universitario de Torrejon, Madrid, Spain (NCT 02,756,143). A complete description of the design and methods of this RCT, was recently published [11]. Our main Objective was to clarify if performing a supervised controlled exercise program throughout pregnancy prevented excessive gestational weight gain. From November 2014 to June 2015, we included a total of 124 pregnant women.

Inclusion criteria were: (I) no obstetric complications according to the American College of Obstetricians and Gynaecologists (ACOG) guidelines [12], (II) gestational age at recruitment <16 weeks, (III) not exercising regularly for more than 30 min (3 days per week), and (IV) able to communicate in Spanish. Exclusion criteria were non-availability to attend to the exercise program during pregnancy or not full filling any of the inclusion criteria.

A simple randomisation was performed with the *Epidat V.3.1* program to allocate the participants into two groups in order of entry: intervention group (IG) and control group (CG). For this, a computer-generated list of random numbers ($n = 200$) was created through the *Epidat* option of balanced groups (similar but not of equal size). Unfortunately, due to the lack of resources, the target number of participant could not be achieved.

Trial coordinators regularly undertook quality control of data handling, and verification of adherence to protocols.

The study was approved by the Local Research Ethics Committee (CEIm Hospital Universitario Severo Ochoa) (19/07/2013). All women gave written consent.

2.2. Maternal and pregnancy characteristics

We recorded the following maternal characteristics: maternal age, maternal weight at 12^{+0}–13^{+5} weeks and height, Body mass index (BMI), racial origin (Caucasian vs non-Caucasian), method of conception (natural or assisted conception), cigarette smoking during pregnancy (yes or no), parity (parous or, according to previous delivery at ≥ 24 weeks' gestation) and gestational age at delivery in days from the last menstrual period calculated by ultrasound.

2.3. Control group

Pregnant women allocated to the CG were advised to do normal daily activity and not to join any educational exercise program including more than 30 min per day at least 3 times per week. The weekly volume of physical activity was monitored by an exercise specialist at a final interview at 38^{+0}–39^{+6} weeks of gestation.

2.4. Intervention programme

The intervention programme was designed according to the 2015 ACOG standards and followed the structure of previous programme studies [12–15]. It consisted in a supervised physical conditioning programme of three-60-minutes-sessions per week during the whole pregnancy (from 12^{+3}–15^{+6} weeks to 38^{+0}–39^{+6} weeks of gestation) at the Hospital gym. Women could attend any of the two evening sessions we offered four days per week, up to a total of three. Each session included 10 min of warming up, 25 min of cardiovascular exercise, 10 min of strengthening exercises, 5 min of coordination and balance, 5 min of pelvic floor exercises and 5 min of stretching and relaxation. Exercises in the supine position were not performed for more than 2 min. Aerobic activity was prescribed at mild to moderate intensity, aiming for 55–60% of maximum heart rate (HR). All women wore a HR monitor (Polar FT7) during the training session to ensure that exercise intensity was mild-moderate and the rating of perceived exertion scale ranged from 12 to 14 (Somewhat Hard) [16].

Weekly volume of physical activity and the percentage of assistance to the program were monitored all throughout the pregnancy by a qualified exercise specialist trained in pre and postnatal exercise.

2.5. Follow-up

Once recruited, both groups had a similar follow-up at the Hospital Universitario de Torrejon. Obstetric appointment took place at 12^{+0}–13^{+5}, 19^{+0}–21^{+6}, 27^{+0}–28^{+6} and 35^{+0}–36^{+6} weeks of gestation. Maternal blood pressure and maternal weight were checked in every visit. Measurements taken at 12^{+0}–13^{+5} week´s appointment were considered as the baseline measurements. Patients were randomized until 15^{+6} weeks of gestation. All patients had a final interview with the exercise specialist at 38^{+0}–39^{+6} weeks´ gestation in other to check their final weight and assess weekly volume of physical activity.

Routine blood routine tests were performed fasting at 10^{+0}–12^{+6} and 34^{+0}–36^{+4} weeks, and not fasting at 24^{+4}–26^{+6} weeks, always in the morning.

Microlife WatchBP Home blood pressure monitor was used for blood pressure assessment. Blood pressure was measured after 5 min of rest in a sitting position, with the arm resting at the level of the heart. Maternal weight was measured in an automatic SECA scale. Blood samples for glucose, Aspartate-amino-transferase (AST), Alanine-amino-transferase (ALT), creatinine and uric acid, were analysed by Dimension EXL (Siemens).

2.6. Study outcomes

Study outcomes were verified by one of three members of the research team (I.F.B., M.B. or A.M.) and are summarized in the following list according to the organ studied.

2.6.1. Cardiovascular

Maternal systolic and diastolic blood pressure measured in mmHg, after 5 min of rest, in sitting resting position, in one arm at heart level, checked at 12^{+0}–13^{+5} (baseline), 19^{+0}–21^{+6}, 27^{+0}–28^{+6} and 35^{+0}–36^{+6} weeks in the obstetric appointment.

2.6.2. Metabolic and hepatic

Maternal weight measured (Kg), checked at 12^{+0}–13^{+5} (baseline), 19^{+0}–21^{+6}, 27^{+0}–28^{+6}, 35^{+0}–36^{+6} and at 38^{+0}–39^{+6} (final weight). Pregnancy weight gain was calculated as the final maternal weight minus the baseline weight.

Fasting blood glucose levels (mg/dl) were measured at the 10^{+0}–12^{+6}- and 34^{+0}–36^{+4} weeks routing blood tests. Blood glucose levels 60 min after a 50 mg Glucose Tolerance Test were measured at the 24^{+4}–26^{+6} weeks routine blood test.

Alanine-amino-transferase (ALT) and Aspartate-amino-transferase (AST) were measured at the 10^{+0}–12^{+6} and 34^{+0}–36^{+4} weeks routine blood test (UI/l) to asses hepatic function and amnio acid metabolism, respectively.

2.6.3. Renal

Serum creatinine and uric acid levels (mg/dl) were determined at the 34^{+0}–36^{+4} weeks routine blood test to asses renal function. Our protocol did not include any earlier analysis.

2.7. Statistical analysis

To describe demographic and clinical characteristics of patients, data were expressed as mean (standard deviation) or median (interquartile range), and proportions (absolute and relative frequencies) as appropriate. Comparisons between treatment groups were performed by ware package SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp) was used for data analysis.

3. Results

A total of 124 women were recruited and randomized into two groups. Seventy pregnant women were randomised to the intervention group (IG) and 54 to de control group (CG). Three women were excluded from the CG: one woman because of a late miscarriage at 20 weeks, other because of high-risk pregnancy (anti-kell antibodies), and the third one withdrew consent after randomization. Additionally, one woman from the IG had non available blood tests results. Twenty-eight women from IG were not compliant with the programme and attended <70% of the programme as requested by the study protocol. A per protocol analysis was finally made with the two final groups: IG ($N = 41$) and CG ($N = 51$), as shown in the Trial Profile (Fig. 1).

The baseline characteristics were similar in both groups. Regarding maternal age, pre-pregnancy BMI, parity, IVF pregnancy, ethnic, previous to pregnancy physical exercise and smoking, both groups were homogeneous (Table 1).

3.1. Cardiovascular outcomes

Both systolic and diastolic blood pressure were studied (Table 2) and no differences were found except at 28 weeks, were systolic blood pressure was lower in the CG compared to the IG (116.31 ± 10.8 mmHg vs. 120.22 ± 10.3 mmHg, $p = 0.010$), but always within normal ranges.

3.2. Metabolic and hepatic outcomes

The evolution through gestation of the maternal weight was analysed and no differences were found between groups (Table 3).

When analysing maternal weight gain during pregnancy, no difference was found. However, there was a tendency for a lower maternal weight at the end of the pregnancy in the IG compared to the CG (10.1 ± 5 Kg vs. 11.4 ± 4 Kg, $p = 0.173$) (Table 3).

Fasting blood glucose level in the first and third trimester, blood glucose after 50 mg glucose tolerance test, AST and ALT levels were similar in both groups (Table 3).

3.3. Renal outcomes

Creatinine and uric acid concentrations in the third trimester were similar in both groups (creatinine 0.57 ± 0.1 mg/dl in the IG compared to 0.59 ± 0.4 mg/dl in the CG, $p = 0.757$; uric acid 3.26 ± 0.6 mg/dl in the IG compared to 3.45 ± 0.7 mg/dl in the CG, $p = 0.218$) (Table 3).

4. Discussion

4.1. Main findings of the study

In this study we found that, first renal, metabolic and hepatic metabolism was similar in pregnant women performing a moderated supervised exercise program compared to controls.

Second, although maternal blood pressure was similar between groups, systolic blood pressure was higher at 27^{+0}–28^{+6} weeks´in pregnant women performing a mild-moderated supervised exercise program compared to controls.

And third, pregnancy weight gain tended to be lower in the exercise group, although we were unable to prove significance.

4.2. Cardiovascular outcomes

Cardiovascular changes have been described in pregnant women under a supervised exercise program during pregnancy [17,18]. Perales et al. [19] described that, pregnant women under a supervised mild exercise program, have significant lower heart rate levels, lower blood systolic and diastolic pressure. Moreaver, a randomized controlled study [5] found that aerobic exercise reduced resting systolic blood pressure in normotensive pregnant women and reflected a positive adaptation of the maternal cardiovascular system. Little is known about the mechanism by which exercise may reduce blood pressure during pregnancy. Exercise has been proposed to reduce oxidative stress, improve endothelial function, as well as immune and inflammatory responses [20,21]. In addition, exercise is associated with an increase on the cardiac output [21]. In our study we were unable to show this effect; in contrast, we found the systolic blood pressure to be higher in the IG at 27^{+0}–28^{+6} weeks. Since this finding sounds clinically implausible, we believe that it merely reflects the result of performing multiple comparisons, more than a real effect of the treatment, unless proven otherwise in another study.

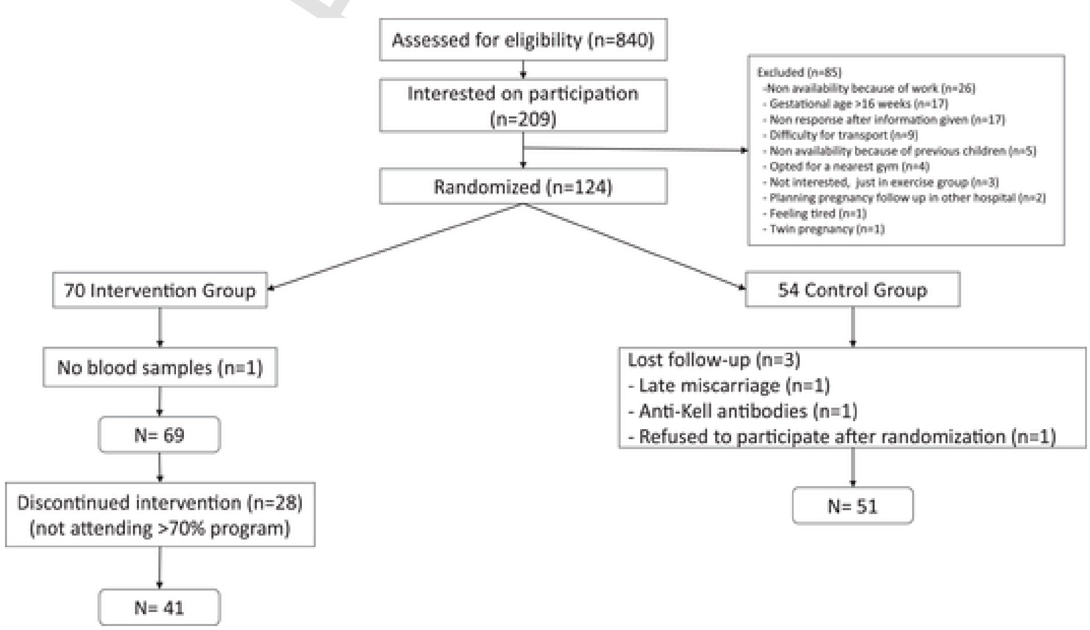

Fig. 1. Flow diagram.

Table 1
Demographic characteristics in both groups.
Data are given as mean and Standard deviation (SD) or n (%). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Intervention Group (N = 41)	Control Group (N = 51)	p value
Maternal age (years)	33.17 (3.19)	32.63 (4.66)	0.510
Maternal 12^{+0}–13^{+5} weeks weight (Kg)	63.65 (10.90)	66.10 (14.56)	0.380
Maternal height (cm)	164.68 (6.89)	164.14 (5.84)	0.682
12^{+0}–13^{+5} weeks BMI	22.81 (3.54)	23.80 (5.09)	0.293
IVF pregnancy	1 (2.4)	2 (3.9)	0.611
Caucasian	41 (100.0)	47 (92.2)	0.067
Pre-pregnancy physical exercise	37 (90.2)	41 (80.4)	0.191
Nulliparous	31 (75.6)	38 (74.5)	0.904
Smoking	10 (24.4)	22 (43.1)	0.061
Gestation time at delivery (days)	278.76 (9.45)	276.08 (11.45)	0.232

Table 2
Cardiovascular outcomes in both groups.
Data are given as mean (Standard deviation). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Systolic Blood Pressure (mmHg)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
12^{+0}–13^{+5} Week	120.54 (10.56)	119.51 (11.26)	0.656
19^{+0}–21^{+6} Week	123.08 (8.99)	120.14 (14.10)	0.254
27^{+0}–28^{+6} Week	122.20 (10.31)	116.31 (10.80)	0.010
35^{+0}–36^{+6} Week	121.27 (8.49)	119.18 (14.60)	0.422
	Diastolic Blood Pressure (mmHg)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
12^{+0}–13^{+5} Week	72.65 (8.70)	73.05 (7.20)	0.813
19^{+0}–21^{+6} Week	72.96 (10.48)	72.25 (6.88)	0.712
27^{+0}–28^{+6} Week	70.92 (11.03)	73.12 (6.90)	0.269
35^{+0}–36^{+6} Week	75.33 (10.81)	74.46 (6.31)	0.653

4.3. Metabolic and hepatic outcomes

Maternal weight gain during pregnancy has an impact on the pregnancy and on the future newborn [22–33]. Previous meta-analysis have demonstrated that exercise can help to prevent excessive weight gain during pregnancy [34–36]. In our study, no differences were found in maternal weight during each visit during pregnancy or in the maternal weight gain at the end of the pregnancy, although a tendency to a lower pregnancy weight gain could be observed in the intervention group. It is true that if we could stratify by basal BMI we may see more pronounced differences in the higher basal BMI group, as demonstrated by some studies [12,37–44], but this sub-group analysis was not possible due to the small sample size.

Glucose is essential for foetal wellbeing [7]. Exercise increases the capitation of glucose by the muscles, and therefore we could argue that the hypoglycaemia that occurs during exercising mothers may influence foetal growth or development. However, our results show no differences in the basal fasting glucose levels between groups. On the other hand, Barakat et al. [10] and Deierlein et al. [45] concluded that regular exercise during pregnancy reduces glucose levels at the screening test for

Table 3
Metabolic, Hepatic and renal outcomes in both groups.
Data are given as mean (Standard deviation). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Weight (Kg)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
12^{+0}–13^{+5} Week	64.89 (11.15)	64.34 (18.65)	0.867
19^{+0}–21^{+6} Week	67.96 (10.66)	70.11 (14.50)	0.430
27^{+0}–28^{+6} Week	71.46 (11.13)	73.66 (14.70)	0.429
35^{+0}–36^{+6} Week	74.48 (11.54)	76.85 (15.05)	0.411
38^{+0}–39^{+6} Week	75.15 (11.57)	76.25 (15.47)	0.705
Maternal weight gain	10.153 (5.39)	11.49 (4.43)	0.173
	Glucose (mg/dl)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
10^{+0}–12^{+6} Week	78.48 (8.34)	76.00 (13.26)	0.305
24^{+4}–26^{+6} Week, 50 g Glucose Tolerance Test	116.23 (35.07)	116.36 (25.98)	0.984
34^{+0}–36^{+4} Week	73.25 (10.27)	73.45 (8.29)	0.920
	AST (UI/ml)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
10^{+0}–12^{+6} Week	15.38 (4.17)	17.33 (7.05)	0.124
34^{+0}–36^{+4} Week	21.65 (5.25)	19.53 (8.32)	0.165
	ALT (UI/ml)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
10^{+0}–12^{+6} Week	27.50 (10.63)	28.27 (11.77)	0.746
34^{+0}–36^{+4} Week	22.93 (9.23)	20.84 (13.49)	0.407
	Creat (mg/dl)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
34^{+0}–36^{+4} Week	0.595 (0.401)	0.575 (0.100)	0.757
	Uric Acid (mg/dl)		
	Intervention Group (N = 41)	Control Group (N = 51)	p value
34^{+0}–36^{+4} Week	3.526 (0.787)	3.262 (0.672)	0.218

nancy does not prevent from gestational diabetes but can help to control glucose levels in diabetic pregnant women [46–48]. In our study, only one woman developed gestational diabetes in the CG, and therefore no comparison could be carried out at this level.

Regarding the hepatic metabolism, it has been described that exercise increases the levels of AST and its activity [49,50]. During pregnancy, it has not been determined how exercise could affect AST and ALT yet. Our results show no statistical changes in the hepatic enzymes during pregnancy in those women exercising compared to controls.

4.4. Renal outcomes

At a renal level, there is no significant effect when performing mild-moderate exercise during pregnancy [8], although it is not clear whether urinary urea nitrogen excretion could be affected by the exer-

4.5. Study strengths and limitations

The main strength of our study resides in being a randomized controlled study with multiple timepoints check-ups. Additionally, the guidelines for exercise followed here are internationally recommended.

On the other hand, the main limitation is the small sample size which may be reason for the lack of beneficial results and did not allow us to perform sub-group analyses. Some may argue that increasing exercise intensity may cause a greater impact, however, high-intensity exercise during pregnancy is related to adverse obstetric outcomes and therefore not recommended [52–56]. Another limitation is the increased proportion of nulliparous women compared to the general low risk pregnant population, which could represent a selection bias. However, parity has not been demonstrated as a risk factor for any of the variables studied. Finally, our study included only low-risk pregnancies and therefore our results might not be valid for a different population.

5. Conclusions

A regular supervised mild-moderate exercise programme during pregnancy does not impact the normal physiological changes that occur during pregnancy. However, further and larger studies are needed to confirm our findings.

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Supplementary materials

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