7 Does physical activity in leisure time early in pregnancy reduce the incidence of preeclampsia or gestational hypertension?

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Acta Obstetricia et Gynecologica Scandinavica
2010; 89: 261–267

ABSTRACT

Objective

Assessment of the association of physical activity in leisure time with preeclampsia and gestational hypertension in the first half of pregnancy in nulliparous women.

Design

Population based prospective cohort study.

Setting

Amsterdam, the Netherlands

Population

All Amsterdam pregnant women between January 2003 and March 2004 who were nulliparous with a singleton pregnancy and delivered after 24 weeks

Design

At their first prenatal care visit women were invited to fill out a questionnaire with sociodemographic and psychosocial variables. Physical activity in leisure time in the past week was measured using questions about walking, cycling, doing sports and other activities in leisure time. The amount of minutes and intensity of each activity was studied using four categories; no, low, moderate or high activity. The 50th and 90th percentiles of the scores of the whole group was used to create these categories. Data from the National Obstetric Register were used for pregnancy outcome. By using multivariate logistic regression we adjusted for sociodemographic and medical confounders.

Main outcome

Incidence of preeclampsia and gestational hypertension

Results

A total of 12.377 women were invited with a response of 67%. 3679 nulliparous women were included. The incidence of preeclampsia and gestational hypertension was 3.5% and 4.4% respectively. The amount of time or intensity of physical activity in leisure time was not associated with a difference in risk of preeclampsia or gestational hypertension.

Conclusion

Physical activity in leisure time early in pregnancy does not reduce the incidence of preeclampsia or gestational hypertension in unselected nulliparous women.

INTRODUCTION

Hypertensive disorders of pregnancy are a leading cause of maternal and perinatal morbidity and mortality worldwide.[1] The origin is thought to be associated with deficient placentation early in pregnancy, which in turn may be caused by immunological, genetic or environmental factors.[2] The expression of the disease is mediated through endothelial dysfunction and increased systemic resistance, resulting in hypertension with a highly variable degree of organ dysfunction of which proteinuria is the most conspicuous. So far no effective treatment is available other than antihypertensive drugs and termination of pregnancy.

Hypertensive disorders in pregnancy and adult cardiovascular diseases share predisposing conditions, like elevated blood pressure and obesity. Protective or disease modifying factors of cardiovascular disease might also be applicable for the prevention of hypertensive disorders in pregnancy. Physical activity is one such factor, known to prevent cardiovascular disease and to reduce its symptoms. Its precise mechanism is unclear, but an acceptable hypothesis is that it mediates a reduction of oxidative stress, which in turn influences the immune response and improves endothelial dysfunction.[3-6] These processes are also involved in the development of preeclampsia and gestational hypertension.[2] Because physical activity is, in part, an external factor, which can be mediated by intervention, its association with preeclampsia and gestational hypertension is vital for the development of non-medical prevention strategies. A number of studies explored the association, but most studies were hampered by the low incidence of preeclampsia, and overall results appear inconsistent.[7-11]

This study investigates the association between physical activity in leisure time early in pregnancy and the development of hypertensive disorders later in pregnancy in an unselected prospective cohort of nulliparous women.

METHODS

The present study is part of the Amsterdam Born Children and their Development study (ABCD-study).[12] This prospective community-based study examined the relationship between various lifestyles during pregnancy and pregnancy outcome in a multicultural population. Between January 2003 and March 2004 12,381 Amsterdam women who attended antenatal care for their first visit were approached by their obstetric caregiver to participate in the study. Within two weeks a questionnaire (pregnancy questionnaire) on sociodemographic characteristics and lifestyle was sent to the pregnant women to

be filled out at home and returned by prepaid mail. Women who gave permission to follow-up received a second questionnaire (infant questionnaire) 3 months after birth concerning pregnancy outcome, lifestyles, and health of the baby. Additional data like pregnancy outcome, infant gender, birth weight and gestational age were obtained from the national obstetric register and the Youth Health Care of the Municipal Health Service in Amsterdam.

Study population

All nulliparous women with singleton pregnancy, who filled out the pregnancy questionnaire before 24 weeks gestational age, who delivered after 24 weeks and gave permission for follow-up were included. The study protocol was approved by the medical ethical committees of all Amsterdam hospitals and the Municipal Privacy Protection Committee of Amsterdam. Participation and permission for data retrieval rested on written consent.

Measurements

Gestational hypertension was defined as a diastolic pressure ≥ 90 mmHg after 20 weeks in a previously normotensive woman. Preeclampsia was defined by the combination of gestational hypertension and proteinuria ≥ 0,3 g/ 24 h or dipstick ≥ ++ after 20 weeks gestation, according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) guidelines.[13] Superimposed preeclampsia was defined as de novo proteinuria ≥ 0,3 g/ 24 h or dipstick ≥ ++ after 20 weeks gestation together with a diastolic pressure ≥ 90 mmHg in women with chronic hypertension. Chronic hypertension was defined as a systolic pressure ≥140 mmHg and/or diastolic pressure ≥ 90 mmHg or the necessity for antihypertensive treatment before pregnancy or before 20 weeks gestational age. Women with chronic hypertension who had a diastolic pressure ≥ 90 mmHg after 20 weeks gestation were included in the gestational hypertension group. The medical files of all women who documented elevated blood pressure in the infant questionnaire or who had a diastolic blood pressure ≥ 90 mmHg and/ or proteinuria in The National Obstetric Register were reviewed for confirmation of the diagnosis preeclampsia or gestational hypertension. If gestational hypertension was diagnosed first and proteinuria occurred later in pregnancy, preeclampsia was the assigned diagnosis. From the remaining women a random sample of 190 women was selected to validate the absence of hypertensive disorders during pregnancy by reviewing their medical records. Physical activity in leisure time in the past week was questioned using four questions about walking, cycling, doing sports and other activities like 'do it yourself' or gardening in leisure time. The amount of time spent in minutes and the intensity (low, moderate or vigorous) was asked. We analyzed the amount of time spent on each activity and the total time spent on physical activity in leisure time. The scores were trichotomized using the

50th and 90th percentiles of the amount of minutes spent on activity of the total group to create four categories. The quantity of minutes spent on each activity was multiplied with the intensity (arbitrarily we coded low by 1, moderate by 2 and vigorous by 3), yielding a numerical score for each activity question, which were summated into a total score. These scores were trichotomized using the 50th and 90th percentiles of levels of intensity of activity of the total group to create four categories;no activity, low activity, moderate activity and high activity.

Characteristics and covariates

Maternal age, gestational age (based on routine ultrasound examination or, if unavailable, on the date of the last menstrual period), birth weight and infant gender were obtained from the Youth Health Care registration of the Municipal Health Service in Amsterdam. All other variables were self reported and defined as follows: maternal education (years of education after primary school; 3 categories: < 5 years; 5-10 years; > 10 years), marital status (married/cohabiting or single), pre-gravid maternal weight and height, previous miscarriage/ abortion (yes or no), smoking during pregnancy (yes or no). Women were asked if they had hypertension, diabetes mellitus or any other disease during their pregnancy, and if they used any medication. Drug utilization was classified according to the International Classification for Primary Care.[14] If women used medication for a specific disease but did not report the disease (for example insulin) they were classified as having the disease (diabetes). Pre-pregnancy body mass index (BMI) was calculated. Missing data on pregravid maternal weight (about 5% compared to 1% general missings) were formally imputed by models using maternal length and parity data, retaining the variability of the data.

Statistical analyses

To compare groups one-way ANOVA with post-hoc Bonferoni analysis or Pearson's chi-square test was used. We estimated the effects of physical activity in the beginning of pregnancy on the incidence of preeclampsia or gestational hypertension later in pregnancy by predefined explorative logistic regression models, with increasing levels of adjustment. First univariate analysis for each variable was used to calculate unadjusted odds ratio's. Subsequently multivariate logistic regression was performed to adjust for medical covariates: BMI, chronic hypertension, diabetes mellitus, previous miscarriage/ abortion, smoking in pregnancy and haemorrhage in the first half of pregnancy (model 1). Those medical covariates that were statistically significant in this analysis were combined with sociodemographic covariates in a second multivariate logistic analysis. Sociodemographic covariates were age, ethnicity, education and marriage/ co-habitation (model 2). The selection of covariates that influenced the model significantly was

performed by back step procedure with the p value for entry set at 0.05 and for removal at 0.10. Women with no physical activity were taken as the reference category. The Hosmer and Lemeshowtest was used to test the goodness of fit of the data. The level of significance used was $p<0.05$. Statistical calculations were performed with SPSS 14.0.2(SPSS Inc.Chicago, IL).

RESULTS

In all, 12,373 women were invited for the ABCD-study and 8266 women returned the questionnaire (response rate 67%). Of these 3679 nulliparous women were included in our study according to our selection criteria. The median gestational age at completing the pregnancy questionnaire was 15.6 weeks (quartiles 14.0-17.3). From the 599 women, who reported elevated blood pressure in the questionnaire or who were coded as such in the national obstetric register, the diagnosis preeclampsia was confirmed in 128 women (3.5%) by reviewing the medical records and gestational hypertension in 161 women(4.4%). Ten medical files could not be retrieved and 300 women had neither preeclampsia nor gestational hypertension. These women were all allocated to the control group. From the 190 women, who were preselected in the control group for confirmation by reviewing medical files, 187 files could be assessed. None of these women had preeclampsia or gestational hypertension during their pregnancy and all were correctly allocated to the control group. All women whose medical files could not be retrieved, were all allocated to the control group. The selection of our study group is described elsewhere using the same cohort for studying the influence of psychosocial stress on preeclampsia and gestational hypertension.[15]

From 80 women (2%), information of physical activity was missing. Demographic and medical characteristics according to degree of physical exercise are presented in Table 1. Women with no or low leisure time physical activities were significantly younger ($p < 0.001$), less often Caucasian ($p < 0.001$), had a higher BMI ($p = 0.005$) and a lower education ($p < 0.001$). Women with no physical activity also smoked more often ($p < 0.001$) and lived more often single ($p < 0.001$). They delivered earlier and birthweight was lower compared tomothers who performed any exercise ($p < 0.001$). Low exercise level was associated with shorter gestational length and lower birthweights compared to moderate but not high exercise ($p < 0.05$). Women with moderate or high total leisure time physical activities were similar for these parameters.

The incidence of preeclampsia and gestational hypertension did not differ between the groups with different total physical activities in leisure time based on time and intensity. After

Table 1. Sociodemographic and medical characteristics of included women according to level and time spend on physical exercise in leisure time in early pregnancy.

	Total group	No exercise	low	moderate	high
N (%)	3679 (100)	454 (12.3)	1502 (40.1)	1322 (35.9)	321 (8.7)
Age (years)	29.9 ± 5.1	27.4 ± 5.4	29.4 ± 5.3	31.1 ± 4.4	31.6 ± 4.2
Etnicity N(%)					
-Caucasian	2461 (66.9)	167 (36.9)	945 (63.0)	1055 (79.8)	263 (81.9)
-Black	157 (4.3)	52 (11.5)	74 (4.9)	22 (1.7)	3 (0.9)
-Turkish/Moroccan	347 (9.4)	93 (20.5)	174 (11.6)	54 (4.1)	9 (2.8)
- Other	712 (19.4)	141 (31.1)	308 (20.5)	191 (14.4)	46 (14.3)
Education N (%)					
-0-5 years	557 (15.2)	123 (27.4)	261 (17.5)	120 (9.1)	21 (6.6)
-6-10 years	1445 (39.6)	239 (53.2)	638 (42.8)	442 (33.6)	99 (31.0)
->10 years	1651 (45.2)	87 (19.4)	593 (39.7)	754 (57.3)	199 (62.4)
Marriage/ co-habitation N (%)					
No	497 (13.5)	99 (21.8)	197 (13.1)	145 (11.0)	50 (15.6)
BMI (kg/m^2)	22.6 ± 3.7	23.3 ± 4.7	22.7 ± 3.8	22.3 ± 3.2	21.8± 2.7
Chronic hypertension N (%)					
Yes	92 (2.5)	16 (3.5)	37 (2.5)	31 (2.4)	4 (1.2)
Diabetes N (%)					
Yes	19 (0.5)	3 (0.7)	10 (0.7)	4 (0.3)	2 (0.6)
Smoking in pregnancy N (%)					
Yes	343 (9.3)	76 (16.7)	141 (9.4)	98 (7.4)	21 (6.5)
Miscarriage/ abortion N (%)					
Yes	969 (26.3)	124 (27.3)	370 (24.6)	360 (27.2)	96 (29.9)
Hemorrhage N (%)					
Yes	431 (11.7)	59 (13.2)	175 (11.8)	153 (11.6)	32 (10.0)
Preeclampsia N (%)	127 (3.5)	20 (4.3)	49 (3.2)	51(3.8)	7 (2.2)
Gestational hypertension N(%)	159 (4.3)	19 (4.1)	77 (5.0)	49 (3.7)	14 (4.3)
Birth weight (g)	3381 ± 557	3229 ± 610	3370 ± 550	3432 ± 543	3346 ± 520
Gestational age (days)	278 ± 14	276 ± 16	278 ± 14	280 ± 13	279 ± 14

Data are expressed as mean ± SD of N (%). BMI: body mass index

adjustment for possible confounders, walking, bicycling, playing sports, other activities or performing any physical activity in leisure time (minutes/week) were not associated with a reduction of preeclampsia (Table 2) or gestational hypertension (Table 3). When women spent more than 585 minutes on physical activities, the adjusted odds ratio was 0.62 (95%CI (confidence interval) 0.25–1.53) for preeclampsia and 0.54 (95%CI 0.22–1.36) for gestational hypertension. Likewise, playing sports or total leisure time physical activities at a high level lacked a significant association with preeclampsia (OR 0.43; 95%CI 0.17–1.10) and gestational hypertension (OR 0.78; 95% CI 0.36–1.69).

Table 2. The association between preeclampsia and sports and total leisure time physical activity in minutes/week or based on intensity and time, calculated by univariate analysis, by multivariate analysis using model 1 and model 2, expressed as odds ratios with 95% confidence limits.

	Controls(%)	PE(%)	Univariate effects	Multivariate effects model 1	Multivariate effects model 2
Sports (minutes/week)					
0	69.8	1	1	1	1
1-70	15.1	16.4	1.09 (0.67–1.77)	1.18 (0.72–1.95)	1.02 (0.61–1.71)
71-180	12.5	10.9	0.88 (0.50–1.56)	0.97 (0.54–1.75)	0.81 (0.45–1.48)
>180	2.6	3.1	1.19 (0.42–3.32)	1.32 (0.46–3.76)	1.04 (0.36–3.00)
Total LTPA (minutes/week)					
0	12.5	15.9	1	1	1
1-235	48.9	48.4	0.78(0.47-1.31)	0.92(0.53-1.60)	0.71(0.40-1.27)
236-585	31.4	29.4	0.74(0.42-1.28)	0.90(0.50-1.64)	0.63(0.33-1.18)
>585	7.2	6.3	0.70(0.30-1.61)	0.88(0.37-2.11)	0.62(0.25-1.53)
Sports					
No sports	69.8	69.5	1	1	1
Low	15.2	14.9	0.98 (0.59–1.62)	1.06 (0.63–1.77)	0.91 (0.54–1.55)
Moderate	12.0	13.3	1.11 (0.66–1.89)	1.22 (0.75–2.10)	1.02 (0.58–1.78)
Vigorous	3.0	2.3	0.80 (0.25–2.56)	0.93 (0.29–3.03)	0.72 (0.22–2.37)
Total LTPA					
No LTPA	12.5	15.9	1	1	1
Low	41.6	38.1	0.72 (0.42–1.23)	0.85 (0.48–1.51)	0.68 (0.38–1.32)
Moderate	36.9	40.5	0.87 (0.51–1.47)	1.04 (0.59–1.85)	0.72 (0.39–1.32)
Vigorous	9.0	5.6	0.48 (0.20–1.16)	0.62 (0.25–1.53)	0.43 (0.17–1.10)

Model 1: BMI, chronic hypertension, diabetes mellitus, previous miscarriage/abortion, smoking in pregnancy and hemorrhage in the first half of pregnancy. Model 2: age, ethnicity, education and marriage/co-habitation. PE, preeclampsia; LTPA, leisure time physical activity; BMI, body mass index

DISCUSSION

We observed no significant association between physical activity in leisure time in early pregnancy and the incidence of preeclampsia and gestational hypertension after appropriate adjustment of covariates. Literature regarding this subject is conflicting. Studies use different methods and definitions which makes it difficult to compare their results.[16] Some studies investigate in particular physical activity at work with or without account for physical activity in leisure time. Most of the studies are retrospective case-control studies. In three retrospective case control studies with data collection by questionnaire after delivery it was observed that leisure time physical activity in the first half of pregnancy was more frequent in controls than in women with preeclampsia.[7;8] More vigorous activity was associated with a lower incidence of preeclampsia.[17] One retrospective cohort study of enlisted active duty military women observed less preeclampsia in nulliparous women

Table 3. The association between gestational hypertension and sports and total leisure time physical activity in minutes/week or based on intensity and time, calculated by univariate analysis, by multivariate analysis using model 1 and model 2, expressed as odds ratios with 95% confidence limits.

	Controls(%)	GH(%)	Univariate effects	Multivariate effects model 1	Multivariate effects model 2
Sports (minutes/week)					
0	69.8	69.4	1	1	1
1-70	15.1	12.5	0.83(0.51-1.35)	0.91(0.55-1.49)	0.77(0.46-1.28)
71-180	12.5	15.6	1.26(0.81-1.97)	1.40(0.89-2.22)	1.18(0.74-1.88)
>180	2.6	2.5	0.96(0.35-2.65)	0.86(0.27-2.80)	0.71(0.22-2.32)
Total LTPA (minutes/week)					
0	12.5	12.0	1	1	1
1-235	48.9	55.7	1.19(0.72-1.97)	1.27(0.75-2.15)	1.01(0.58-1.75)
236-585	31.4	27.2	0.90(0.52-1.57)	1.00(0.56-1.77)	0.71(0.39-1.30)
>585	7.2	5.1	0.73(0.32-1.70)	0.73(0.30-1.79)	0.54(0.22-1.36)
Sports					
No sports	69.8	69.4	1	1	1
Low	15.2	14.4	0.95 (0.60–1.50)	1.03(0.64–1.65)	0.87(0.54–1.41)
Moderate	12.0	11.3	0.94 (0.57–1.57)	1.06(0.63–1.79)	0.90(0.53–1.52)
Vigorous	3.0	5.0	1.70 (0.81–3.59)	1.75(0.79–3.90)	1.43(0.64–3.20)
Total LTPA					
No LTPA	12.5	12.0	1	1	1
Low	41.6	48.1	1.21 (0.72–2.02)	1.26 (0.74–2.16)	1.02 (0.58–1.78)
Moderate	36.9	31.0	0.88 (0.51–1.51)	0.97 (0.56–1.71)	0.69 (0.38–1.26)
Vigorous	9.0	8.9	1.02 (0.50–2.07)	1.12 (0.53–2.34)	0.78 (0.36–1.69)

Model 1: BMI, chronic hypertension, diabetes mellitus, previous miscarriage/abortion, smoking in pregnancy and hemorrhage in the first half of pregnancy. Model 2: age, ethnicity, education and marriage/co-habitation. GH,gestational hypertension; LTPA, leisure time physical activity; BMI, body mass index

employed in jobs involving high levels of physical activity compared to nulliparous working at low levels of physical activity.[18] Contrary to these studies one other retrospective case-control study of nulliparous women observed that women with clerical work experienced less frequently preeclampsia than women with moderate to high physical activity at work, after adjustment for age, BMI, smoking and social status.[19]

Three prospective cohort studies with assessment of physical activity in leisure time early in pregnancy also showed different results.[9-11] Saftlas et al. observed a non-significant reduction of the incidence of preeclampsia. The extent of the risk reduction was comparable to our findings. Magnus et al. found a significant reduction when there were ≥ 25 physical activities per month. Osterdal et al. studied the largest cohort and investigated time, intensity and metabolic equivalents. Although this study did not observe an association between leisure time activity and the incidence of preeclampsia, those women who spend ≥ 270 minutes on physical activity per week had an odds ratio of 1.7

for severe preeclampsia. The precise definition of severe preeclampsia was not reported. In our study physical activity levels in women with preeclampsia < 34 weeks were not different from women with preeclampsia ≥ 34 weeks.

A recent Cochrane review could identify two trials (total n=45) randomising women to participate in an exercise program or not.[20] These studies were too small to draw conclusions regarding the prevention of preeclampsia or gestational hypertension, as only one case of preeclampsia was encountered. One of the two identified studies observed that diastolic blood pressure was lower in the exercise group, which supports a positive effect.[21] A literature search using the terms used in this Cochrane review detected one new study. This study had not enough statistical power to detect a difference in the incidence of preeclampsia. [22]

In practice the low incidence of preeclampsia precludes randomised studies using this endpoint. Case control studies with retrospective design are prone to recall bias as the data have to be collected after delivery. Prospective cohort studies, like the present one, beginning in early pregnancy have the advantage that recall bias is minimised, but the inclusion of a large number of women is needed. But lack of power, especially in groups with high physical activity, is a serious threat even of fairly large cohort studies, due to the low prevalence of (severe) preeclampsia and low frequency of intense physical activity.

A potential bias in case-control and cohort studies is that women who exercise probably differ from women who do not. In our study 70 % did not practice any kind of sports while 13 % did not practice any physical activity at al. In the Danish cohort of Odenthal 63 % of the women did no sportive activity at all. We adjusted our analysis with a number of covariates that have been well described by others to be associated with gestational hypertension or preeclampsia.[2;23] However, certainty that adjustment was adequate can never be obtained.

Assessment of physical activity is complicated because there is no 'gold standard' and unequivocal norm. Self report may suffer from recall bias. Therefore questionnaires focus on discrete activities like sport and activity at work which are easy to recall, and less subject to interpretation as 'physical activity'. Activity monitors are more objective and could reduce report errors but these are not suitable for prospective studies with a large sample size like our study.[24] Hence our approach was questionnaire-based with self-reporting. Existing questionnaires were unacceptably long. Therefore we used our own questionnaire. If anything, our measurement of leisure time may have been subject to random error, although the current results most likely will not alter with more extensive measurement.

Even if preventive physical programs are considered, practical constraints can be expected. It is generally assumed that disturbed placental development in early pregnancy

is an important factor in the origin of preeclampsia and gestational hypertension.[2] If the promotion of physical activity can reduce the incidence of preeclampsia and gestational hypertension than the first half of pregnancy is likely the most effective period. At this early stage of pregnancy women are often easily tired and generally abstain from high activity.

CONCLUSION

Physical exercise in leisure time in early pregnancy is not associated with reduced incidence of preeclampsia and gestational hypertension in an unselected nulliparous population. An effect of high physical activity can not be excluded because of the low incidence of high physical activity and the low incidence of preeclampsia.

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