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**REPERCUSSÕES MATERNAS E PERINATAIS DO
EXERCÍCIO E DA ATIVIDADE FÍSICA NA GESTAÇÃO**

Dissertação de Mestrado

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REPERCUSSÕES MATERNAS E PERINATAIS DO EXERCÍCIO E DA ATIVIDADE FÍSICA NA GESTAÇÃO

KARINA TAMY KASAWARA

Dissertação de mestrado apresentada ao programa de Pós-Graduação em Tocoginecologia, da Faculdade de Ciências Médicas, da Universidade Estadual de Campinas, para obtenção do título de Mestre em Ciências da Saúde, área de concentração em Saúde Materna e Perinatal, sob a orientação do Prof. Dr. João Luiz de Carvalho Pinto e Silva.

Campinas, 2012

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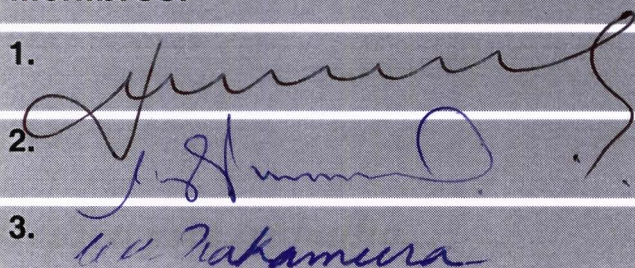
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**Curso de Pós-Graduação em Tocoginecologia da Faculdade
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Dedico este trabalho...

*à minha mãe Neusa,
pela educação e por ter-me ensinado,
com sua postura de mulher virtuosa e profissional,
a valorizar o meu ofício e a amar incondicionalmente.*

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Símbolos, Siglas e Abreviaturas

AIG	– Adequado para a idade gestacional
BE	– Bicicleta estacionária
CAISM	– Centro de Atenção Integral à Saúde da Mulher
CEP	– Comitê de Ética em Pesquisa
ECA	– Ensaio controlado aleatorizado
FCM	– Faculdade de Ciências Médicas
GIG	– Grande para a idade gestacional
GC	– Grupo-controle
GE	– Grupo-estudo
HAC	– Hipertensão arterial crônica
IC	– Intervalo de confiança
IMC	– Índice de Massa Corporal
kg/m²	– Quilograma(s) por metro(s) quadrado(s)
mg	– Miligrama(s)
mm Hg	– Milímetro(s) de Mercúrio
OR	– <i>Odds Ratio</i>
p	– Nível de significância
PE	– Pré-eclâmpsia
PIG	– Pequeno para a idade gestacional
PNAR	– Pré-Natal de Alto Risco
PNE	– Pré-Natal Especializado
RN	– Recém-nascido
TCLE	– Termo de Consentimento Livre Esclarecido
UNICAMP	– Universidade Estadual de Campinas
UTI	– Unidade de Terapia Intensiva
%	– Porcentagem

Resumo

Introdução: A pré-eclâmpsia (PE) é um dos principais distúrbios hipertensivos da gestação e representa a principal causa de mortalidade e morbidade materna e perinatal. A atividade física e os exercícios físicos vêm sendo descritos para a prevenção da PE. Na gestação sem risco e/ou de baixo risco podem trazer benefícios para a saúde materna, além de ser considerados atividade segura para a saúde da mãe e do feto. No entanto, pouco se sabe sobre seu real efeito, principalmente na gestação de alto risco. **Objetivo:** revisar, de forma sistemática, a literatura sobre o efeito do exercício físico e da atividade física no desenvolvimento da PE. Avaliar a associação do exercício físico com bicicleta estacionária (BE) em gestantes com hipertensão arterial crônica (HAC) e/ou PE prévia, com o tipo de parto, repercussões maternas e neonatais. **Sujeitos e métodos:** Para a revisão sistemática foram utilizadas as bases de dados: PubMed®, Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), Scientific Eletronic Library On-line (SciELO), Physiotherapy Evidence Database (PEDro) e ISI web of KnowledgeSM. Através dos descritores: “exercise”, “motor activity”, “physical activity”, “pre-eclampsia”, “eclampsia”, “hypertension, pregnancy-induced”, sem restrição de ano de publicação e idioma. Para avaliar a associação do exercício físico com BE e o tipo de parto, repercussões maternas e neonatais, foi realizado um ensaio controlado aleatorizado (ECA), entre janeiro/2008 e novembro/2011, no Hospital da

Mulher Professor Doutor José Aristodemo Pinotti – CAISM, com 116 gestantes com HAC e/ou PE prévia. As participantes foram aleatorizadas em: grupo-estudo (GE), em que realizaram exercícios físicos com BE semanalmente, sob supervisão de um fisioterapeuta, durante 30 minutos, com intensidade leve e controlada; grupo-controle (GC), em que seguiram a rotina de assistência pré-natal. Os dados referentes ao parto, às repercussões maternas e neonatais foram coletados dos prontuários. A análise da revisão sistemática foi realizada por meio do programa *Comprehensive Meta-Analysis*. O ECA foi analisado por intenção de tratamento, e o risco relativo foi calculado para as principais variáveis. O nível de significância assumido foi de 5%. **Resultados:** Foram incluídos 17 estudos na revisão sistemática: 6 do tipo caso-controle, 10 coortes e 1 ECA. Conforme a análise dos artigos do caso-controle, observou-se o efeito protetor da atividade física. Dentre os artigos de coorte e do estudo ECA não foi observada diferença significativa. No ECA deste estudo, a média de sessões de exercício físico realizado pelo GE foi de 9,24 sessões. Não foram observadas diferenças entre os grupos, com relação às variáveis: tipo de parto, indicações para a via alta de parto e repercussões maternas, incluindo a morbidade materna e internação na Unidade de Terapia Intensiva (UTI). As repercussões neonatais (peso do RN, adequação do peso à idade gestacional, idade gestacional, índice de Apgar, internação do UTI, morbidade neonatal) não foram diferentes entre os grupos. **Conclusão:** A revisão sistemática indicou efeito protetor da atividade física de lazer para a prevenção da PE. Já o exercício físico com BE, em gestantes com HAC e/ou PE prévia, realizado sob supervisão profissional, uma vez por semana, não apresentou risco materno e neonatal para ocorrência de morbidade e internação na UTI.

Summary

Introduction: Preeclampsia (PE) is a major hypertensive disorder of pregnancy and represents the leading cause of maternal and perinatal mortality and morbidity. Physical activity and exercise have been described for the prevention of PE. During pregnancy without risk and/or low risk may benefit for maternal health, and are considered safe activity for the mother and fetus health. However, it is not known about the real effects, mainly in high-risk pregnancy. **Objective:** The aim of the study was to review the literature on the effect of exercise and physical activity and the development of preeclampsia (PE). Assess the association of exercise with stationary bicycle (SB) in pregnant women at risk for developing PE with the type of delivery, maternal and perinatal outcomes. **Subjects and methods:** For the systematic review we used the following databases: PubMed®, the Latin American and Caribbean Health Sciences (LILACS), Scientific Electronic Library Online (SciELO), Physiotherapy Evidence Database (PEDro) and ISI Web of Knowledge. Through the keywords "exercise", "motor activity", "physical activity", "pre-eclampsia," "preeclampsia," "hypertension, pregnancy-induced" without restriction year of publication and language. To evaluate the association of exercise with the type of delivery, maternal and perinatal outcomes, we performed a

randomized controlled trial (RCT), between january/2008 and november/2011 at Women's Hospital Prof. Dr. José Aristodemo Pinotti - CAISM with 116 pregnant women at risk for PE (chronic hypertension, previous PE or both factors). Participants were randomized in the study group (SG) performed exercise with SB weekly under the supervision of a physiotherapist for 30 minutes with mild intensity and controlled; the control group (CG) followed the routine prenatal care. Data related to delivery, the maternal and perinatal outcomes were collected from medical records. The significance level was 5%. **Results:** We included 17 studies in the systematic review: 6 case-control, cohort and a 10 RCT. According to the analysis of case-control items observed protective effect of physical activity. Among the articles in the study cohort and RCT was not significant difference. In our RCT, the average exercise sessions conducted by SG was 9.24 sessions. No differences were observed between groups regarding the variables: type of delivery, indications for route of delivery and high maternal effects, including maternal morbidity in Intensive Unit Care (ICU). The repercussions of neonatal (birth weight, adequacy of weight to gestational age, gestational age, Apgar scores, admission to the ICU, neonatal morbidity) were not different between groups. **Conclusion:** The systematic review indicated the protective effect of leisure physical activity for prevention of PE, observed in case-control studies. Since physical exercise with SB, in patients with CH and/or previous PE, under professional supervision, once a week, did not show risk for occurrence of maternal and neonatal morbidity and hospitalization in ICU.

1. Introdução

A gestação causa alterações anatômicas e fisiológicas no corpo da mulher. A maioria apresenta aumento de peso, assim como aumento do gasto energético em repouso. Além disso, ocorrem alterações endócrinas que modificam o seu metabolismo corporal e o sistema cardiovascular. Essas alterações ocorrem progressivamente, ao longo da gravidez, variando com a idade gestacional (1).

A prática do exercício físico é recomendada na gestação sem risco e/ou baixo risco por trazer benefícios para a saúde materna, além de ser considerada atividade segura para a mãe e para o feto, principalmente quando realizada com orientação e supervisão profissional (2-4).

Conforme recomendações do Colégio Americano de Ginecologia e Obstetrícia (ACOG) (5), a prática de exercício físico com intensidade moderada pode ser realizada todos os dias ou pelo menos três vezes na semana, mesmo em gestantes previamente inativas. No entanto, mulheres sedentárias devem iniciar aumentando gradualmente a duração e frequência de suas atividades para até 30 minutos por sessão, estratégia considerada segura e eficaz para promover a saúde materna e do feto, sem prejuízos (4,6).

Deve-se considerar que exercícios realizados com a ação da gravidade, ou seja, em que as gestantes necessitam de controle postural, o gasto energético é elevado quando comparado com o de outras modalidades, como natação e bicicleta estacionária. Esse fato se intensifica com o aumento do peso corporal e a evolução da gestação (1).

Ao iniciar estas atividades, devem-se tomar alguns cuidados para realizá-las de forma adequada, de acordo, preferencialmente, com os critérios estabelecidos pelo ACOG (5), que determina contraindicações absolutas para exercício na gestação em casos de:

- Doença cardíaca significativa
- Doença pulmonar restritiva
- Incompetência istmo-cervical
- Gestação múltipla de risco para trabalho de parto prematuro
- Sangramento persistente no 2º ou 3º trimestre de gestação
- Placenta prévia
- Trabalho de parto prematuro durante a gestação atual
- Ruptura prematura das membranas
- Pré-eclâmpsia

O ACOG preconiza contraindicações relativas para realização de exercícios no período da gestação (5) para:

- Anemia severa
- Arritmia cardíaca materna não avaliada
- Bronquite crônica
- Mau controle do diabetes tipo 1
- Obesidade mórbida extrema

- Desnutrição extrema ($IMC < 12 \text{ kg/m}^2$)
- Estilo de vida extremamente sedentário
- Restrição de crescimento fetal na gestação atual
- Mau controle hipertensivo
- Limitações ortopédicas
- Mau controle de crises convulsivas
- Hipertireoidismo mal controlado
- Tabagista severa

Por este motivo, recomenda-se que as gestantes iniciem qualquer atividade física somente com a autorização médica. Do mesmo modo, com relação à modalidade, devem tomar alguns cuidados especiais, como evitar certos tipos de exercícios que as exponham a risco como quedas, lesões musculoesqueléticas ou que diminuam sua segurança e a do conceito.

1.1. Exercício físico nas desordens hipertensivas em mulheres não gestantes

Em estudos de metanálise de ensaios controlados, o exercício físico regular com intensidade moderada vem sendo descrito como um aliado no tratamento das desordens hipertensivas (7-9).

O exercício físico, quando realizado com frequência regular, provoca adaptações autonômicas e hemodinâmicas que influenciam o sistema cardiovascular (10). No entanto, além do exercício físico, outras questões como alimentação, obesidade e principalmente o estilo de vida são fatores que influenciam no quadro clínico das desordens hipertensivas (11,12).

O exercício físico é recomendado para prevenção, tratamento e controle da HAC, indicado para ser realizado por pelo menos cinco vezes na semana, com duração de 30 minutos cada sessão, e intensidade moderada (13).

Considerando que o exercício físico favorece hipertensas, não gestantes, acredita-se que os exercícios e as atividades físicas possam minimizar os efeitos das desordens hipertensivas durante a gestação, inclusive prevenir e reduzir a incidência da pré-eclâmpsia (PE) e suas complicações (14-17).

1.2. Pré-eclâmpsia

A PE é um dos principais distúrbios hipertensivos da gestação e representa a principal causa de mortalidade e morbidade materna e perinatal (18). O processo da doença pode ter início durante a fase de implantação do tecido trofoblástico, seguido de uma significativa resposta inflamatória sistêmica que se estende durante todo o período gravídico-puerperal. Essa resposta causa reações maternas imprevisíveis e variáveis que, quando não assistidas e convenientemente controladas, podem provocar efeitos deletérios sobre os diversos sistemas, principalmente vascular, hepático, renal e cerebral (14, 19, 20).

A PE é diagnosticada após a vigésima semana gestacional, sendo caracterizada pelo aumento da pressão arterial sistólica ($\geq 140\text{mmHg}$), diastólica ($\geq 90\text{mmHg}$) e presença de proteinúria ($\geq 300\text{mg}$ no período de 24 horas) (21,22) A etiologia da PE não está estabelecida; no entanto, existem hipóteses relacionadas à consequência do desenvolvimento anormal da placenta, à presença de fatores de predisposição constitucional materna, estresse oxidativo,

má adaptação imunológica e suscetibilidade genética. Esses fatores associados podem promover a disfunção endotelial, repercutindo em sintomas hipertensivos já no estágio avançado da gestação (14).

As desordens hipertensivas durante a gestação representam as principais causas de morte materna, principalmente em países em desenvolvimento. Na América Latina e no Caribe, a porcentagem de mortalidade materna é de 26%, comparada a 16% em países desenvolvidos (23).

Estudo realizado nas capitais brasileiras e no Distrito Federal apontou que os transtornos hipertensivos lideram as causas de morte, representando em torno de 25% dos óbitos maternos no Brasil (24). Apesar da redução significativa a cada triênio, os índices de mortalidade materna no estado do Paraná relativos à PE representam a principal causa de morte materna, responsável por 18% dos óbitos (25). Embora estes números sejam inferiores aos apresentados no Sudeste do país, ainda assim, dentre as causas de morte materna diretamente relacionadas a fatores obstétricos, a hipertensão foi a mais frequente, com 23,3% na cidade de São Paulo (26) e 31% em Campinas (27).

A mortalidade materna é um dos principais indicadores da qualidade de assistência à saúde das mulheres e, conseqüentemente das condições de vida e saúde geral da população, o que evidencia, de modo muito preciso, as diferenças socioeconômicas dos países (26).

Recente revisão sistemática e metanálise de ensaios controlados aleatorizados referente ao efeito do uso de antioxidantes com as vitaminas C e

E durante a gestação concluiu, em amostra de 19.810 mulheres, que esta providência não apresentou os resultados imaginados na prevenção da PE ou qualquer outra intercorrência materna ou perinatal, corroborando com outros estudos da literatura (28-30).

Alguns estudos associam o uso das aspirinas (ácido acetilssalicílico) com a redução da ocorrência de PE (31-34); em contrapartida outro estudo refere a não associação ou influência das aspirinas com desfechos neonatais favoráveis (30).

O carbonato de cálcio é associado ao efeito protetor na prevenção da PE (33, 35), no entanto, sem benefícios adicionais nas repercussões neonatais (35, 36).

1.3. Atividade física e exercício físico na prevenção da pré-eclâmpsia

Atividade física é definida como qualquer movimento corporal voluntário que resulte em gasto energético maior que o gasto em repouso (37); exercício físico é definido como toda atividade física estruturada, planejada e repetida, que tem por objetivo a melhoria da saúde e manutenção de um ou mais componentes da aptidão física (38). Alguns estudos que objetivam a melhora da capacidade física referem que quando alguma atividade é realizada com frequência planejada, inserida no contexto da vida diária com o aumento proposital do consumo do gasto energético, como ir andando até o trabalho, também pode ser caracterizada como exercício físico.

O exercício físico inicialmente foi descrito como forma de tentar prever a ocorrência de PE. Os estudos avaliavam a variação da frequência cardíaca

(FC) e da pressão arterial (PA) e tentavam associar essa variação com a ocorrência de PE, pois quanto maior a variação da FC em repouso com o pico da FC durante o esforço físico, maior seria a chance de desenvolver hipertensão gestacional (39,40) e PE (41- 45).

Atualmente, acredita-se que a prevenção da PE, através de exercícios físicos, pode ocorrer devido à redução dos níveis pressóricos e do condicionamento cardiovascular das gestantes (46). Além disso, sabe-se que podem diminuir a concentração materna de substâncias oxidantes, reduzir a resposta inflamatória que acompanha a doença, estimular a vascularização e o crescimento placentário, além da reversão da disfunção endotelial (16,47).

Estudos que analisam o efeito da atividade física como formas de prevenção para a PE avaliam diversas modalidades, como as atividades ocupacionais (48-51), as de lazer e/ou recreacional (49, 52-59), e o exercício físico regular com propósito terapêutico (60,61).

No entanto, não existe consenso quanto ao real efeito do exercício físico na prevenção da PE (61,62).

1.4. Atividade física durante a gestação de baixo risco e as repercussões neonatais

O exercício durante a gestação não deve ameaçar a hígidez do conceito, ou provocar sofrimento fetal. Um estudo de revisão sobre o efeito da atividade física no peso ao nascer, prematuridade e restrição de crescimento fetal não detectaram associação significativa. A análise da revisão apoia a hipótese de

que tanto o excesso como o déficit de atividade física poderiam tornar-se prejudiciais ao binômio mãe-feto (63).

Quando a atividade física relaciona-se às atividades ocupacionais, alguns estudos apresentam informação de risco para prematuridade e baixo peso ao nascer, a depender do tipo da jornada de trabalho [longas jornadas de trabalho (64-66), do esforço físico intenso (67), dos turnos noturnos de trabalho (68), e outras condições de trabalho (64,69,70)]. Da mesma maneira, algumas condições ocupacionais podem repercutir nos desfechos neonatais, como recém-nascidos pequenos para a idade gestacional (66, 71).

Recente ensaio clínico que avaliou, em gestantes sedentárias, o efeito do exercício aeróbico por meio da dança e do alongamento por 60 minutos, duas vezes na semana, e mais 30 minutos de exercícios em domicílio em dias alternados, quando comparado com um grupo-controle, não mostrou associação com peso ao nascer e taxa de prematuridade (72).

Considerando a alta prevalência de gestantes com hipertensão arterial crônica (HAC) e história obstétrica de PE, que apresentam risco para desenvolver a PE na gestação atual, entende-se ser relevante avaliar a associação do exercício e da atividade física com o tipo de parto, repercussões maternas e perinatais. A identificação de qualquer associação entre esses eventos poderia ser útil na orientação e prescrição apropriada de exercícios físicos para as gestantes com risco aumentado para PE. A indicação do exercício físico direcionado a essas gestantes poderia levar à prevenção da PE e da morbidade e mortalidade materna e neonatal relacionada.

2. Objetivos

2.1. Objetivo geral

Avaliar a associação do exercício e da atividade física durante a gestação com as repercussões maternas e perinatais.

2.2. Objetivos específicos

- Revisar a literatura, de forma sistemática, sobre o efeito do exercício e da atividade física na prevenção da pré-eclâmpsia.
- Identificar as características das atividades a serem realizadas para possível prevenção da pré-eclâmpsia, de acordo com os estudos revisados da literatura.
- Avaliar a associação do exercício físico com bicicleta estacionária em gestantes com hipertensão arterial crônica e/ou pré-eclâmpsia prévia com: tipo de parto, repercussões maternas (internação na Unidade de Terapia Intensiva e as morbidades no parto e pós-parto) e repercussões neonatais (peso do recém-nascido, idade gestacional, adequação à idade gestacional, índice de Apgar no primeiro e quinto minutos, internação do recém-nascido na Unidade de Terapia Intensiva e morbidades neonatais).

3. Publicação

3.1. Artigo 1

Exercise and physical activity in the prevention of preeclampsia: systematic review

Submetido à revista Acta Obstetricia et Gynecologica Scandinavica

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Exercise and physical activity in the prevention of preeclampsia: systematic review

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Abstract

Background: Exercise and physical activity have been studied and suggested as a way to reduce or minimize the effects of preeclampsia. **Objectives:** The aim of this study was to evaluate the association between exercise and/or physical activity and occurrence of preeclampsia. **Data source:** We conducted electronic searches without year of publication and language limitations. **Methods of study selection:** This is a systematic review designed according to PRISMA. Different databases accessed: PubMed[®], Latin-American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library On-line (SciELO), Physiotherapy Evidence Database (PEDro), ISI web of KnowledgeSM. Using the *Medical Subject Headings* (MeSH): (“exercise” OR “motor activity” OR “physical activity”) AND (“preeclampsia” OR “eclampsia” OR “hypertension, pregnancy-induced”). Inclusion criteria were studies conducted in adults who were engaged in some physical activity. The selection and methodological evaluation were carried out by two independent reviewers. Risk assessment was made by the odds ratio (OR) and incidence of preeclampsia in the population who performed physical activity/exercise. **Results:** 231 articles were found, 214 were excluded based on title and full-text. 17 articles remained. Comparison six case-control studies physical activity had a protective effect on the development of preeclampsia (OR= 0.77, 95%CI 0.64-0.91, $p<0.01$). The 10 prospective cohort studies showed no significant difference (OR= 0.99, 95%CI 0.93-1.05, $p=0.81$). The only randomized clinical trial showed that the stretching group had a protective effect on the development of preeclampsia (OR=6.34, 95%CI 0.72-55.37, $p=0.09$). **Conclusions:** This systematic review indicates a trend towards a protective effect of physical activity on the prevention of preeclampsia.

Keywords: pregnancy, systematic review, physical activity, exercise, preeclampsia

Introduction

Physical activity (PA) is recommended during pregnancy because it may be beneficial to maternal health. Furthermore, it is considered a safe activity for the mother and fetus (1, 2).

The American College of Obstetricians and Gynecologists (3) recommends moderate intensity physical exercise every day or at least three times a week, even in pregnant women who were previously inactive (4,5).

Exercise and PA have been studied and suggested as a way to reduce or minimize the effects of preeclampsia (PE) associated with the prevention and reduction in its incidence or recurrence (6-9). Hypertensive disorders are among the leading causes of maternal morbidity and death, especially in developing countries. However, few well-characterized methodological studies were proposed (10).

Exercise may contribute to a reduction in blood pressure levels and cardiovascular conditioning in pregnant women (11). It may protect against preeclampsia by reducing the maternal concentration of oxidative substances (oxidative stress); stimulating vascularity and placental growth and preventing endothelial dysfunction (12).

Due to the lack of consistent data on this topic, we have proposed a systematic review to focus on the effect of exercise and PA on the prevention of preeclampsia and its complications.

For this review, we considered exercise as any structured, planned and repetitive form of physical activity, aimed at improving health and maintaining one or more components of physical fitness. PA was defined as any voluntary bodily movement that increased energy expenditure above the basal level (calories expended in the resting state) such as leisure-time or recreational activities, occupational activities, planned physical exercise

(sports) (13). The main objective of this study was to evaluate the association between exercise and PA and the development of PE. An additional objective was to recognize the characteristics of activities that could be considered to possibly prevent PE.

Sources

This is a systematic review on the effect of exercise and physical activity on the prevention of PE. It was registered at the site PROSPERO (<http://www.crd.york.ac.uk/prospero/>): CRD42012001975.

Inclusion criteria for this analysis were studies conducted in adult humans, with no known disease, who were engaged in some form of PA in order to evaluate the incidence of PE, without limitation to year of publication (up to June, 2011) and language. We considered PA as any voluntary bodily movement that increased energy expenditure above the basal level, such as leisure-time or recreational activities, occupational activities and planned physical exercise (sports) (13).

Research was carried out by a systematic search in different databases: PubMed[®], Latin-American and Caribbean Literature in Health Sciences (LILACS), Scientific Electronic Library On-line (SciELO), Physiotherapy Evidence Database (PEDro), ISI web of KnowledgeSM. Databases were accessed using the *Medical Subject Headings* (MeSH): (“exercise” OR “motor activity” OR “physical activity”) AND (“preeclampsia” OR “eclampsia” OR “hypertension, pregnancy-induced”).

Study selection

The selection and methodological evaluation of the articles were carried out by two independent reviewers. Initially, the articles were screened by analyzing their titles

and/or abstracts. Articles that did not meet the inclusion criteria were excluded. Then full-text articles that potentially addressed the topic were accessed. References of the remaining articles were reviewed to identify articles that were not located due to a limited search strategy. When there was a lack of consensus between the two reviewers, a third reviewer was consulted to help overcome disagreement. Data retrieved from selected studies was adapted for use based on a World Health Organization form (WHO) (14).

When studies did not show sufficient data to conduct this review, additional information was extracted from the authors of primary studies by electronic contact before study exclusion.

Risk assessment and comparison of clinical outcome was made by the odds ratio (OR) and incidence of PE in the population who performed physical activity and/or physical exercise.

For data analysis, the Comprehensive Meta-Analysis program, version Evaluation (15) was used. The incidence of PE and lack of PE was extracted from studies of groups engaged in physical activity and those who did not take part in any activity. When exercise or physical activity was categorized into yes or no, this value was considered for analysis. When activities were analyzed in different categories, the reference value (none) was considered *versus* the sum of PE incidence in the remaining categories. The results of these articles were grouped according to type of study, comparing odds ratio (OR) values and generating a final odds ratio with a 95% confidence interval. Then articles reporting occupational activities and pre-pregnancy activities were analyzed separately among each type of study to observe their effect on the development of PE.

Results

Starting from a limited search strategy, databases were accessed following a sequence. First, the PubMed[®], next step was to access the Latin American and Caribbean Literature in Health Sciences (LILACS) database and the Scientific Electronic Library On-line (SciELO) database, followed by the Physiotherapy Evidence Database (PEDro) and ISI Web of KnowledgeSM database. When duplicate studies appeared, we considered the first database found. Literature search produced a total of 231 articles, with 49 in PubMed, seven in LILACS and 175 in ISI.

Of these articles, 178 were excluded based on title, since they did not fulfill the predefined inclusion criteria; twenty were excluded for reasons of patent publication, 15 because they were bibliographic reviews; 143 because of failure to satisfy the topic (Figure 1).

After evaluating the abstracts, we observed that 5 were duplicate studies. An article was published twice in different journals (16, 17). Another was published twice by the same journal, although in different editions (18, 19). The abstracts of two other articles were published in annals of conferences and later the full-text article was published with complete data (20-23). One article referred to a letter mentioning the original article (24, 25). Only one of the two duplicate articles was included.

Twenty-four studies that did not meet the inclusion criteria were excluded. Five other studies were also excluded because they reported a physical exertion test for assessment of variation in blood pressure as a way to predict PE. As a result, 19 full-text articles remained to be analyzed.

After full-text analysis, two other studies were excluded for not showing consistent data to analyze. Electronic contact with the main authors was attempted with no success (26, 27). For final analysis, 17 articles remained.

The remaining articles were classified according to type of study: six were case-control studies, 10 were prospective cohort studies and one was a randomized clinical trial. Table 1 summarizes the main characteristics and the results of articles included.

When six articles of case-control studies were grouped to compare the participation or lack of participation in PA despite diverse types and intensities, it was observed that PA has a protective effect of around 23% on the development of PE (OR= 0.77, 95%CI 0.64-0.91, $p=0.00$) (21, 28-32) (Figure 2). However, in this type of study, when analyzed separately there was an increased risk of PE in women who performed labor activities in both two studies reporting occupational activity (OR=1.62, 95%CI 1.09-2.42, $p=0.01$) (29, 30) (Figure 3).

Analyzing the period of exposure to PA in two case-control studies which evaluated participation in PA in the prepregnancy period, it was demonstrated that exercises performed in the year before pregnancy exerted a protective effect on the development of PE (OR= 0.56, 95%CI 0.41-0.76, $p=0.00$) (21,31) (Figure 4).

Of the 10 articles representative of the prospective cohort studies, two (19, 33) failed to show the precise data of women with PE. Since the Comprehensive Meta-Analysis program allows the direct inclusion of the odds ratio values, the study power was calculated proportionally to other studies and the results of ten studies was compared (17,23,34-39). On data comparison, however, there was no difference between PA and lack of PA (OR= 0.99, 95% CI 0.93-1.05, $p=0.81$) (Figure 5). We separately analyzed an article reporting that occupational activity posed a risk for the development of PE (OR=1.28, 95%CI 0.92-1.77, $p=0.13$) (40). Regarding the prospective cohort studies in which exposure to PA occurred before pregnancy, we observed that there was no difference (OR= 0.85, 95%CI 0.67-1.09, $p=0.21$) (23, 36, 37) (Figure 6).

The only randomized clinical trial found in this review evaluated the repercussion of a moderate intensity 40-minute walking exercise program, five times per week versus a low intensity 40-minute stretching exercise program, five times per week. The pregnant women began activity at 18 weeks gestation. A comparison between the walking group and the stretching group showed that the stretching group had a protective effect on the development of PE (OR=6.34, 95%CI 0.72-55.37, p=0.09) (40).

The intensity of PA was difficult to evaluate, due to the variety of methods used. The included studies quantified and grouped PA intensity as low, medium and high (29,36,38); by a scale of perceived exertion (31,34), by the time engaged in activity (week/month) (17,21,23,28), by the number of times the activity was practiced per week or month (32,35,37,40), employed or unemployed status (30,39) or according to the type of activity performed (19,33).

Discussion

The results of this systematic review indicate that the performance of recreational and sports PA has a protective effect on the development of PE when analyzing case-control studies, both in exercises performed during pregnancy and in the prepregnancy period. Concerning cohort studies, although some studies demonstrated that PA may exert a protective effect against PE, when their results were combined this association was not confirmed. Clinically, women have to be encouraged to perform exercise and increase their recreational PA during pregnancy to improve maternal health, including a possibility to prevent PE.

This review shows different types of studies with diverse methodologies, making data analysis more difficult. These differences are determined by different statistical powers, types

of activities, intensities and periods of exposure to physical activity or exercise. Furthermore there are differences in the diagnosis of PE, for example, when comparing the Royall College of Obstetricians and Gynaecologists (RCOG) and the Medical Society of Obstetrics Australia and New Zealand (SOMANZ) with the Society of Obstetricians and Gynecologists of Canada (SOGC) and the American Society of Hypertension (ASH) (41). However, not all articles include information about how the diagnosis of PE has been made.

The scarcity of randomized clinical trials precludes adequate assessment of the effect of an intervention on a certain outcome. The only clinical trial found and included in this systematic review did not show statistically significant results. According to Yeo (40), a limitation of their study is the sample size analyzed that do not represent a $p < 0.05$ and power > 0.80 .

The lack of clinical trials on this topic led us to review case-control studies. The design of these studies, however, has many limitations because it depends on a well-limited selection of cases and controls. Furthermore, subject selection may suffer influence from a variation in PE incidence in the study population, making exposure to exercise difficult to assess (42).

Cohort studies are considered ideal to investigate the incidence and natural history of a disease, despite difficulty in the control of variation in the exposure factor which may lead to bias. Measurement units of occupational and leisure-time PA during pregnancy are difficult to control (43).

Characteristics of physical activities and PE

During the selection process of the articles included in this review, we noticed that there was no standardization regarding the definition of PA and physical exercise. Constant conflict has been created because these terms are sometimes interchangeably

used. Studies analyzed showed a variety of PA, such as occupational activities (29,30,32,39) leisure-time and/or recreational activities (17,21,23,28,30,31,35,36,38), general physical activities (19,33) and physical exercise as sports activities (37,40). There is still heterogeneity among the methods used to assess physical activity. Information was collected by the use of questionnaires, face-to-face interviews and database analysis. Results may be compromised by different frequencies, intensities and duration. The actual effect on the research objective analyzed was difficult to evaluate.

In the review conducted, two case-control studies (29,30) assessing occupational activity and a single cohort article (39) reporting that this activity was associated with the risk of developing PE, corroborated with the findings in a review by Bonzini (44). According to that author, risk was possibly associated with long working hours, long periods standing at work and work activity involving considerable physical exertion, particularly at the end of pregnancy. However, the type of occupational activity and risk intensity for this affirmation could not be assessed because the evaluation of activities did not use the same standard and precluded a comparison.

A cohort study by Chang (39) assessed work schedule, hours of work per week, type of occupational activity, type of industry, corporate work and workplace schedule, using a population database named the “The Taiwan Birth Cohort Study.” In contrast, Spinillo (29) formally analyzed the employed or unemployed, type of job, job sector and occupational activity, body position at work, physical intensity level, working hours per week, time since quitting work and social class of the partner, using a structured questionnaire in pregnant women with severe PE compared to normotensive nulliparous women. This methodology differs from that of Saftlas (30) who evaluated hours of work spent standing, walking and sitting, comparing sedentary occupational activities to non-

sedentary occupational activities. Time at work spent sitting was assessed by interview. In this case, employment status was classified as employed or unemployed.

Nevertheless, unemployed pregnant women were not necessarily less active than employed pregnant women. Unemployed woman can perform housework that involves greater physical exertion than a person who spends a large amount of time sitting during a working day. That is why it is so difficult to measure the amount of activity at work, during leisure-time activities or at home doing daily chores.

Considering the diversity of PA in a woman's life, leisure-time activities play a fundamental role during pregnancy. It represents changes in physical and mental behavior are introduced during this particular time in a woman's life regardless of the quantity of PA that had been performed previously (45).

Intensity

The impact of exercise and PA on the cardiovascular system varies according to the type, duration and level of intensity. Assessment of PA intensity may be performed by measuring the variation in heart rate (HR) increase with exertion compared to the HR at rest or to maximum heart rate (or peak rate). However, only Yeo (40) measured the impact of PA on the cardiovascular system. The risk of developing PE seems to be reduced with increasing intensity of PA and energy expenditure (21,23, 28). However, in this review the intensity of PA could not be adequately analyzed, since each study used a different methodology for assessment.

Period of exposure to exercise

Both case-control studies evaluating prepregnancy PA showed a significant protective effect on the development of PE. Sorensen (2003) categorized women into two groups

(inactive and active) according to participation in leisure-time PA during the year before pregnancy. An interview was conducted in the beginning of pregnancy, which was known to be the most appropriate procedure. Rudra (2005) interviewed women in the immediate postpartum period about perceived exertion (Borg scale) in recreational PA performed during the 12 months before pregnancy, categorizing PA in a variety of ways: none to weak (reference), moderate, strenuous and very strenuous to maximal (21,31). (Figure 3). Prospective cohort studies did not show any difference, highlighting that there were differences in the activities analyzed. Hegaard (36) assessed the total quantity of PA including sports, gardening and walking, classified as sedentary, light and moderate-to-heavy and did not find any significant difference due to the small amount of women engaged in moderate-to-heavy activities. Rudra (23) evaluated participation in recreational activity, classified as none or any activity. Tyldum (37) investigated the frequency, intensity and duration of exercise such as walking, swimming or participation in sports, although he did not specify the pre-gestational period evaluated.

However, a reduction in PA is virtually always present during pregnancy. In a study by Evenson (46), 13% of pregnant women in the USA practiced PA before pregnancy, although PA was discontinued at the beginning of pregnancy. Similarly, Owe (47) observed that 46.4% women in Norway exercised before pregnancy and this number decreased to 28% at 17 weeks of gestation. Despite these studies, Evenson (46) observed that 35% of women exercised before pregnancy and continued to exercise throughout pregnancy.

When evaluating participation in recreational activities during the year before and in the first 20 weeks of gestation, Sorensen (21) observed that categories such as “before only” and “during only” did not represent protection against PE, while engaging

in PA during both periods showed a risk reduction of 41%, compared to sedentary women before and during pregnancy (OR=0.59, 95%CI 0.35-0.98). Previously active women should be stimulated to maintain the level of PA during pregnancy, and women who were previously sedentary should be encouraged to begin to perform regular physical exercise with a gradual increase in intensity as recommended by ACOG (3).

In conclusion, our study indicates a protective effect of physical activity on the prevention of PE. It was observed that leisure-time or recreational physical activity were associated with a protective effect. Unfortunately, due to heterogeneity in study results, the optimum intensity of recreational PA that ensures a protective effect on the development of PE could not be assessed. The occupational activity represented risk for occurrence of PE and has to be studied and analyzed separately the others types of PA. However, further studies with well defined methodological designs are required to strengthen the evidence that PA and regular physical exercise during pregnancy may have a protective effect against PE.

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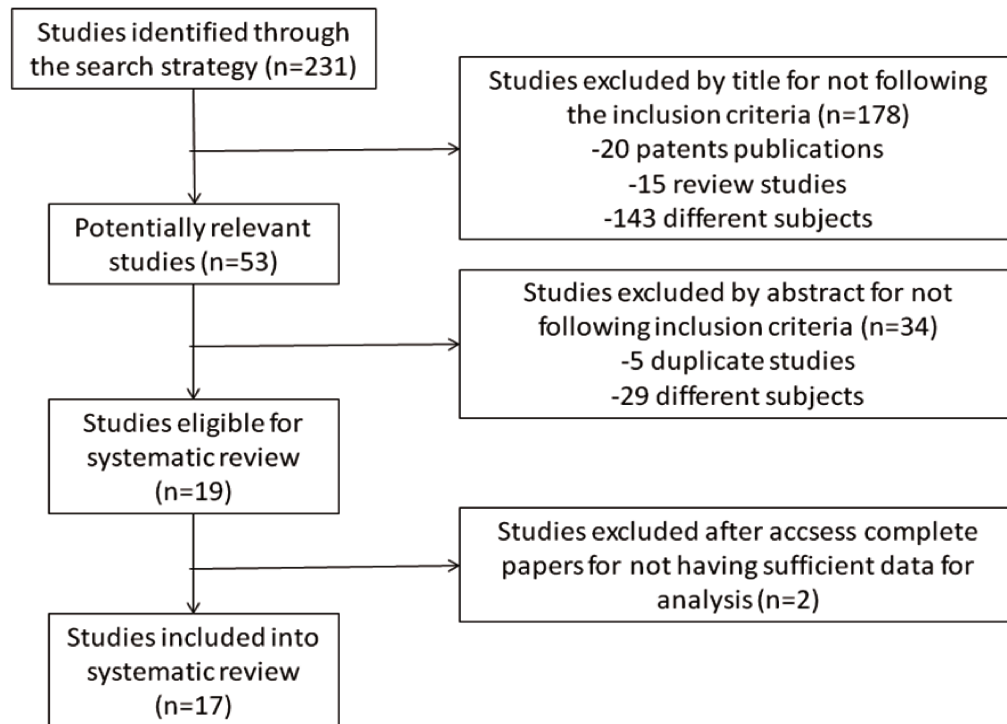
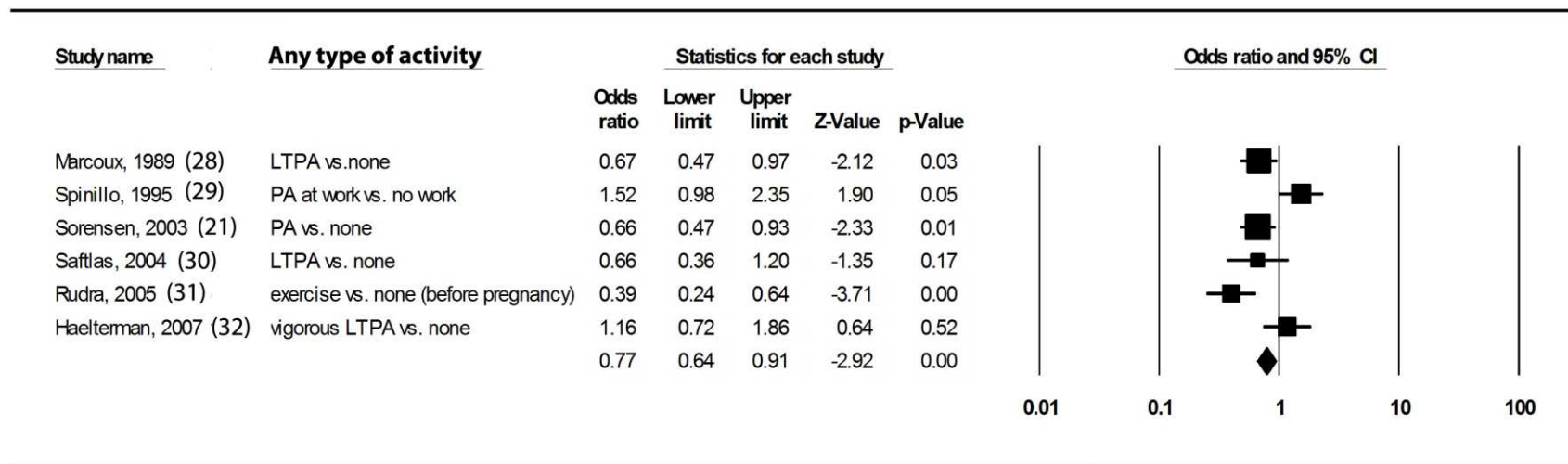


Figure 1: Flow chart of study selection process.



PA = physical activity
LTPA = leisure time physical activity
vs. = versus

Figure 2: Forest plot of the risk of PE for any type of physical activity *versus* no physical activity in case-controls studies.

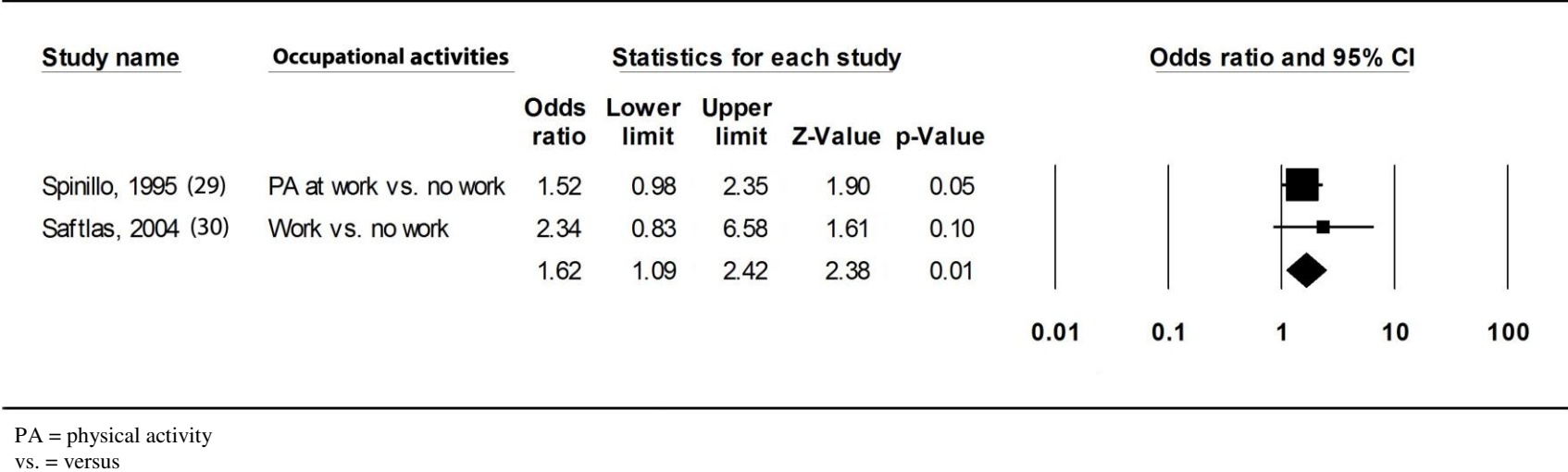
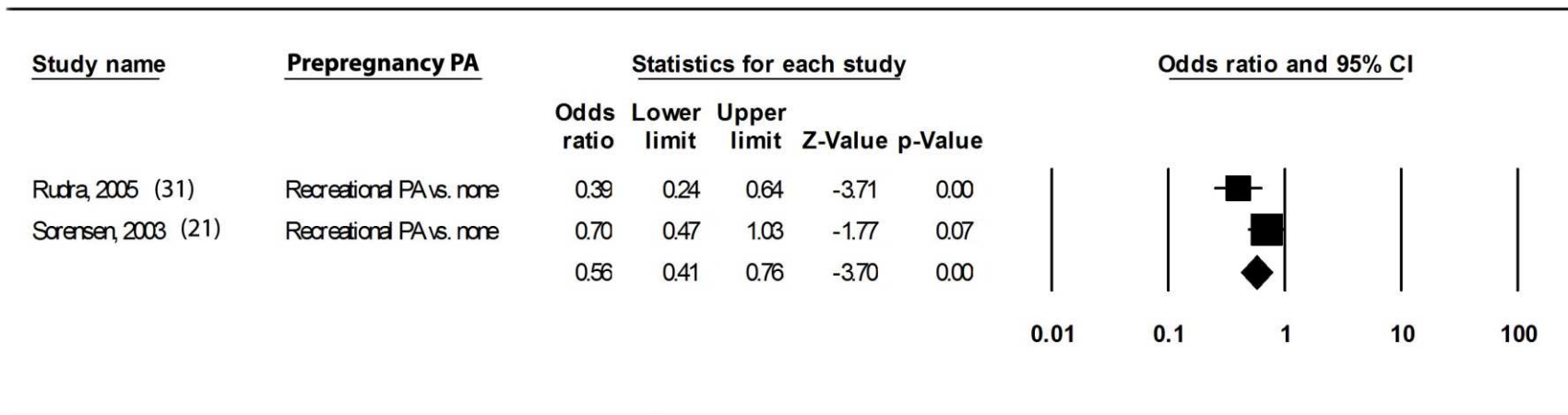
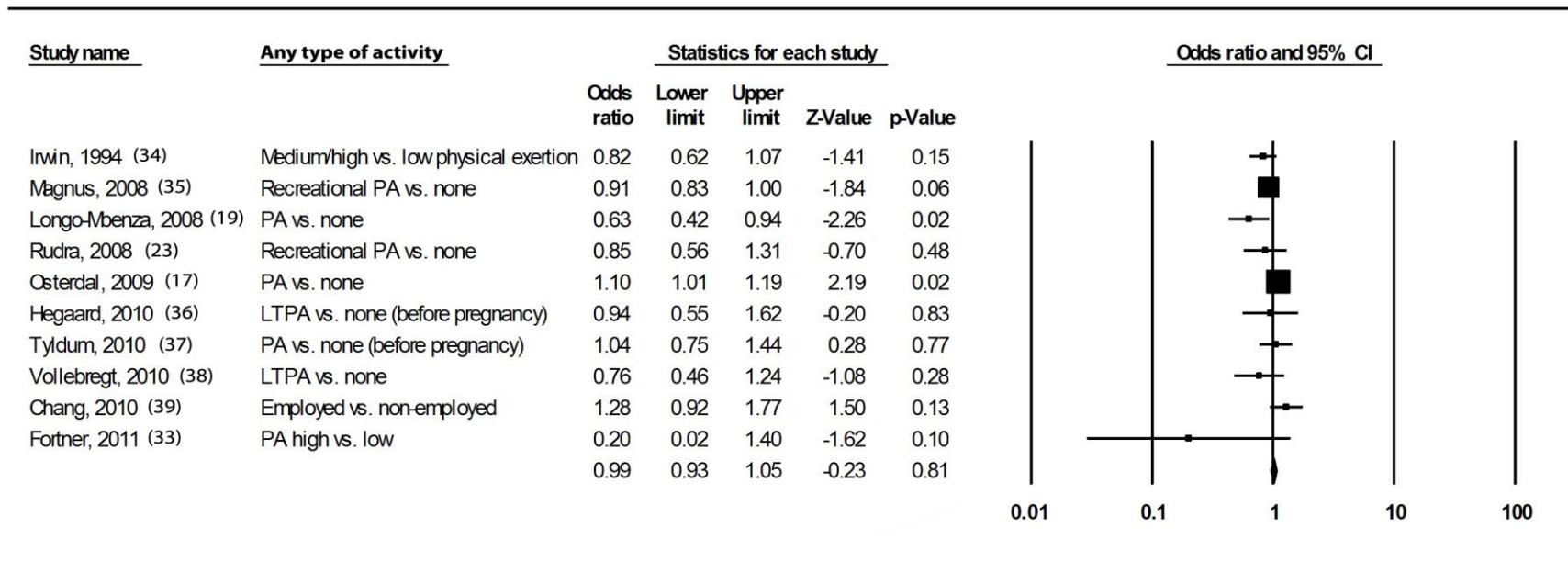


Figure 3: Forest plot of the risk of PE for occupational activities in case-controls studies.



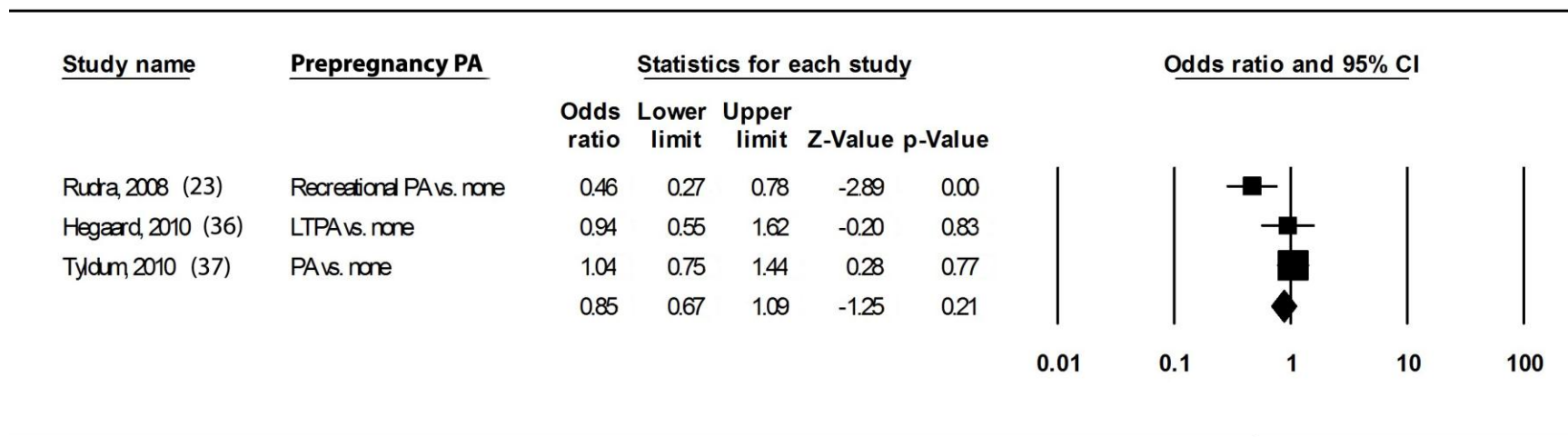
PA = physical activity
vs. = versus

Figure 4: Forest plot of the risk of PE for prepgnancy PA in case-controls studies.



PA = physical activity
LTPA = leisure time physical activity
vs. = versus

Figure 5: Forest plot of the risk of PE for any type of physical activity *versus* no physical activity in cohort studies.



PA = physical activity
LTPA = leisure time physical activity
vs. = versus

Figure 6: Forest plot of the risk of PE for prepregnancy PA in cohort studies.

Table 1. Summary of studies involving exercise as preventing the development of preeclampsia

Autors / Year	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Marcoux et al., 1989	Case-control	172 PE, 254 gestational diabetes and 505 controls	Interview with questionnaire at hospital a few days after delivery records of Retrospective Case-Mix	Risk of PE and GH	LTPA, walking (frequent vs. Not frequent) and standing position (hours/day) during a regular workday on first 20 wk gestation	Standing position not associated with PE or GH; frequent walking associated with a reduced risk of PE (OR 0.6, 95% CI 0.4-0.9) but not with GH
Irwin et al., 1994	Cohort	5605 enlisted active duty military women	Analysis System (RCMAS), a database of the Defense Manpower Data Center	PIH, hypertension complicating pregnancy, mild or unspecified, severe PE, eclampsia	Occupational exposures: PA classified by job title during pregnancy	Nulliparas had a significantly increased risk ratio for PIH (RR=2.3). nulliparas employed in jobs involving high levels of PA were at significantly decreased risk of PIH (construction craftsmen, RR=0.37; unskilled laborers RR=0.71). Physical exertion at medium intensity had a high risk ratio for PE (RR=2.5)
Spinillo et al., 1995	Case-control	160 severe PE and 320 controls	Interview with questionnaire administered at birth	Relation between PA and PE	Four-level scores of PA, type of work, physical intensity (sedentary, moderate or intense), posture and work hours on the first trimester of pregnancy	Moderate or high level of PA associated with PE compared to mild activity (OR 0.2, 95% CI 1.11-3.88)
Sorensen et al., 2003	Case-control	201 PE and 383 controls	Structured questionnaire during postpartum hospital stay	PE risk	Recreational activities, frequency and average time spent, walking pace, distance and stair climb on first 20 wk of pregnancy and before pregnancy	During pregnancy: any recreational activity (OR 0.66 CI 0.47-0.94). The time per wk with PA was inversely related PE risk (p trend= 0.018). Vigorous activities (0.46 CI 0.27-0.79). Decreased PE risk with increasing energy expend PA > 31.5 MET h/wk 0.44 CI 0.23-0.84 p=0.010. Stair climbs daily was inversely associated p= 0.039. Before pregnancy: vigorous PA OR 0.40 CI 0.23--0.69. PA during both period (OR 0.59 CI 0.35-0.98)
Saftlas et al., 2004	Case-control with prospective data collection	44 PE, 172 GH and 2422 controls	Face-to-face interview before 16 wk gestation	Relation between type of job, exercise or sports, LTPA and PE	Time at work spent sitting, standing and walking; women with sedentary work vs. Non-sedentary work; proportion of the time spent sitting; exercise or sports once per wk for the 12 months before pregnancy; LTPA; calories expended on LTPA before 16 wk of gestation	Non significant reduction in risk of PE in non-sedentary jobs and in the low or moderate sitting categories; GH not associated

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Autors/ Year	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Rudra et al., 2005	Case-control	244 PE and 470 controls	Structured questionnaire on post-partum hospital visits	PE risk	Perception of exertion, intensity and energetic of PA at the year prior pregnancy	The intensity of recreational PA is strongly and inversely related with PE risk. Moderate exertion referent no or weak OR 0.54 CI 0.26-1.12. Strenuous exertion OR 0.2 CI 0.11-0.44. Statistically significant inverse trend: perceived exertion (p<0.001); energy expenditure (p=0.01).
Haelterman et al., 2007	Case-control	102 PE, 99 GH and 4381 controls	Interview by telephone	PE and GH risk	Work schedule, postures, physical exertion, breaks, workspace, job strain, social support and environmental exposures; time spent sitting, standing and walking; frequency pushing or pulling objects, carrying or lifting loads and stair climbing in a workday	Standing daily at least 1 hour consecutively without walking had a higher risk of PE [OR 2.5, 95% CI (95%) 1.4-4.6]. As the same climbing stairs frequently (OR 2.3, 95% CI 1.2-4.1) and women working more than 5 consecutive days without a day-off (OR 3.0, 95% CI 1.0-9.5)
Longo-Mbenza et al., 2008	Prospective cohort	238 black pregnant	Questionnaire about PA and consumption of vegetables and meat	PIH: PE, transient or GH	PA: intense activity (farmers, manual workers), inactivity (sedentary professions) first trimester of pregnancy	Active pregnant shows more protection against PE (RR=0.63, 95% CI 0.33-0.94)
Magnus et al., 2008	Cohort	59573	Questionnaire about PA	PE risk	Recreational PA (brisk walking, running, bicycling, attendance at training studios, prenatal aerobics classes, low-impact aerobics classes, high-impact aerobics classes, dancing, skiing, team sports, swimming, walking, horseback riding or other). 14-22 gestational wk	For PE comparing women who exercise 25 times or more per month with inactive women OR 0.79 (95% CI: 0.65-0.96). The association was strongest among women who BMI was less than 25kg/m ² comparing as the higher than 30kg/m ² .
Rudra et al., 2008	Cohort	2241 pregnant women who began PN care before 16wk, spoke and read English, >18yr	Structured interview-administred questionnaire in early pregnancy	Incidence of PE	PA the year before and during early pregnancy, around 7 days before interview (15.1wk)	111 developed PE. No association between PA during a week in early pregnancy and PE Risk OR 1.07 CI 0.67-1.69. Any PA year before pregnancy OR 0.55 CI 0.30-1.02. time spent and energy expenditure were not associated with PE risk. No PA before and early pregnancy vs. only before OR 0.73 CI 0.30-1.77 vs. during both 0.76 CI 0.34-1.73 vs. only pregnancy 2.03 CI 0.71-5.81.

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Autors/ Year	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Yeo et al., 2008	Randomized clinical trial	41 walking group, 38 stretching group	Subjects did exercise at home five times a wk and reported to the Women's Health Exercise Lab (WHEL) once a wk	Incidence of PE and GH in walking and stretching group	40 minutes of exercise (walking or stretching) five times a wk, starting at 18 wk gestation until the end of pregnancy 18 gestation wk until the end of pregnancy	The difference in the risk for PE in the two groups was no significant (p=0.110); the stretchers were 1.8 times as likely to develop GH as the walkers (95% CI 0.89-3.61) but not significant
Østerdal et al., 2009	Prospective cohort	85139	Telephone interview	PE and severe PE	Exercise reported (0, 1-44, 45-74, 75-149, 150-269, 270-419, ≥420 minutes/wk) At the 12 and 30 gestation wk	270-410 and ≥420 minutes/wk were associated with increased risk of severe pre-eclampsia (OR=1.65, 95%, CI 1.11-2.43; OR=1.78, 95%, CI 1.07-2.95)
Hegaard et al., 2010	Prospective	2793 women	Questionnaire about the year before pregnancy	PE risk	LTPA classified as: sedentary, light, or moderate-to-heavy the year before pregnancy	Moderate-to-heavy LTPA had more tendency a lower risk of PE (OR=0.6 , 95% CI 0.3-1.4)
Tyldum et al., 2010	Cohort	3656	Questionnaire about PA	PE risk	PA (frequency, intensity, duration) pre-pregnancy	No link between pre-pregnancy PA and PE. Women physically active for 120 min/wk or more had tendency for reduced risk for PE (adjusted OR 0.6: 95% CI 0.3-1.2)
Vollebregt et al., 2010	Prospective cohort/ population based	3679 pregnant women in Amsterdam between Jan 2003 and Mar 2004 with a singleton pregnancy and who delivered after 24 wk	Questionnaires at the first prenatal visit	incidence of PE and GH	PA in leisure time (walking, cycling, playing sports and others activities), time spent in minutes and the intensity (low, moderate and vigorous). PA in early pregnancy (past wk- around 15.6 wk)	Incidence of PE was 3.5% and GH 4.4%. The amount of time or intensity of LTPA was not associated with difference in risk of PE or GH. Women spent more 585 min OR 0.6 CI 0.25-1.53 PE and 0.54 CI 0.22-1.36 GH. Playing sports or total LTPA at high levels 0.43 CI 0.17-1.10 PE and 0.78 0.36-169 GH.

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...conclusion

Autors/ Year	Study design	Sample size	Data collection	Outcome	Exposure definition and period of exposure	Results
Chang et al., 2010	Prospective cohort	20276 post-partum women	Home interview using a structured questionnaire 6 months post-partum	Incidence of PE and GH	Maternal employment during pregnancy (work schedule, working hours per wk, job title, type of industry, ownership of work and scale of workplace) during pregnancy	1.8% with GH, 0.8 with PE and 61% (12404) worked during pregnancy. There were no statistically significant difference between non-employed and work schedule and work hours for the incidence of PE and GH. GH: Non-emp 1.7% emp 1.8 OR 1.12 CI 0.90-1.39) adjusted OR 0.98 CI 0.78-1.24; PE: non-emp 0.7% emp 0.9% OR 1.27 CI 0.91-1.77 adjusted OR 1.09 0.76-1.55.
Fortner et al., 2011	Prospective cohort	1043 self-identified Hispanic pregnant women, age 16-40, singleton pregnancy, no prior hypertension or diabetes	interview at prenatal care and from medical records after delivery	incidence of PE and hypertensive disorders (GH and PE)	PA by Kaiser PA Survey (KPAS) stratified in four domains: occupational activities, participation in sports and exercise, active living habits and household and family care activities early pregnancy (since onset up time of interview) and during the year before pregnancy	4.8% hypertensive disorders (HD) and 2.9% PE. Decrease the risk of hypertension disorders with increase sports/exercise in early pregnancy (p trend 0.04). High level active living activity (OR 0.4 CI 0.1-1.1 p=0.007) and household/care giving activities (0.4 CI 0.1-1.3 p=0.07) associated 60% reduction HD relative to low levels. High level total PA were associated with 70% decreased HD (OR 0.3 CI 0.1-1.0 p=0.06). No association with pre-pregnancy PA.

OR: odds ratio; PE: preeclampsia; PA: physical activity; LTPA: leisure time physical activity; wk: weeks; GH: gestational hypertension; PIH: pregnancy-induced hypertension; BMI: body mass index; emp: employed; Non-emp: non employed

3.2. Artigo 2

Maternal and perinatal outcome of exercise in pregnant women with chronic hypertension and/or previous preeclampsia: a randomized controlled trial

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Dear Mrs. Karina Tamy Kasawara:

This acknowledges the receipt of your submission entitled, "Maternal and perinatal outcome of exercise in pregnant women with chronic hypertension and/or previous preeclampsia: a randomized controlled trial," to the American Journal of Obstetrics & Gynecology.

If any items in the submission checklist were omitted, the submission will be considered incomplete and returned to you for resubmission. It is the responsibility of the corresponding author to make sure all authors have been consulted and have approved this submission. We appreciate your attention to these important details.

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Thank you for your submission to the American Journal of Obstetrics & Gynecology.
Sincerely,

Tom Garite, MD
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Editor-in-Chief

Maternal and perinatal outcome of exercise in pregnant women with chronic hypertension and/or previous preeclampsia: a randomized controlled trial

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The authors report no conflict of interest.

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Abstract

OBJECTIVE: The aim of the study was to evaluate the association between physical exercise supervised in pregnant women with chronic hypertension and/or previous preeclampsia and maternal and neonatal outcome. **STUDY DESIGN:** A randomized controlled trial conducted between January 2008 and November 2011, at Women's Hospital Professor Dr. José Aristodemo Pinotti – CAISM, enrolled 116 pregnant women with chronic hypertension and/or previous preeclampsia, considered risk for preeclampsia development. They were randomized in two groups: a study group (SG), performed a physical exercise with a stationary bicycle once a week, during 30 minutes, the intensity was controlled (heart rate 20% above resting values), under professional supervision; or a control group (CG), not engaged in any physical exercise. The data was retrieved from the medical charts. The significance level assumed was 5%. **RESULTS:** The mean number of physical exercise sessions performed by the 58 pregnant women from the SG was 9.24 ± 7.03 . There were no differences between groups comparing type of delivery and maternal outcomes, including maternal morbidity and hospitalization in the Intensive Unit Care; and neonatal outcomes, birth weight, adequacy of weight to gestational age, prematurity, Apgar scale at the first and fifth minutes, hospitalization in the Intensive Unit Care and neonatal morbidity. **CONCLUSION:** Physical exercise using a stationary bicycle in pregnant women with chronic hypertension and/or previous preeclampsia, performed once a week, under professional supervision, did not interfere in the delivery method and did not produce maternal and neonatal risk for the occurrence of morbidity.

Key words: pregnancy high risk, motor activity, birth weight, hypertension pregnancy-induced.

Introduction

Hypertensive disorders during pregnancy are major causes of maternal deaths worldwide, particularly in developing countries. Hypertensive disorders are responsible for 26% of maternity deaths in Latin America and in the Caribbean, in comparison to 16% in developed countries (1). A study carried out in several Brazilian capitals and in the Federal District indicated that hypertensive disorders are a leading source of mortality, accounting for about 25% of maternal deaths in Brazil (2). Despite a significant triennial reduction of maternal mortality in some states, these rates are still high in the majority of these Brazilian states. In one state in the Southern region of Brazil, preeclampsia(PE)/eclampsia was the main cause of maternal death and it was responsible for 18% of all deaths registered (3). In the Southeastern region, an area where comparative mortality rates are usually lower than in other regions, hypertensive disturbances were the most common disorders among the causes directly related to obstetrical factors, responsible for 23.3% of all deaths (4), as registered in the city of São Paulo.

It is well-known that pregnant women with chronic hypertension (CH), or those who already had PE in previous pregnancies, have an increased recurrence risk of PE in subsequent pregnancies and have several other related clinical and obstetrical complications (5-7). Among these complications are a higher probability of repeat PE, higher rates of operative deliveries, neonatal hospitalization in intensive therapy units (ICU) (8), lower gestational age, low birth weight and lower weight percentile at birth (5,9).

With the aim of preventing or mitigating comorbid conditions, rest is usually recommended for these pregnant women. However, there is insufficient

scientific evidence to recommend systematic rest, as a method to prevent PE development and its complications (10).

Exercise and physical activity are associated with a reduced risk and treatment for hypertension in nonpregnant women (11). The practice of physical exercise is also recommended in a no risk and/or low-risk pregnancy because of its benefits to maternal health. In addition, exercise is considered a safe activity for both the mother and the fetus, especially when performed under professional guidance and supervision (12-14). In low-risk pregnant women, when low-intensity and moderate-intensity exercise is performed, it does not alter newborn (NB) weight (12, 15-17) and reduces the risk of prematurity (18, 19). However, little is known about the effects of physical exercise during a high-risk pregnancy and its impact on the mother and newborn.

More recently, recommendations for exercise in pregnant women with hypertension or at risk for PE development were initiated, aimed at minimizing the deleterious effects of hypertensive disorders in pregnancy, including the prevention and reduction of the incidence of PE (20-23). PE could be prevented through supervised physical exercise by reducing blood pressure levels and promoting better cardiovascular fitness in pregnant women (24). In addition, exercise may decrease maternal concentration of oxidative substances, stimulate placental vascularization and growth; and act on the reversal of endothelial dysfunction (25).

Physiologically, the performance of physical exercise during pregnancy offers benefits. Furthermore, it is well-known that physical activity has an important role in hypertensive individuals. It remains to be elucidated whether the performance of physical exercise is not associated with a higher fetal maternal risk in

pregnant hypertensive women or those at risk for developing the disease. The aim of the present study was to evaluate the association between physical exercise supervised in pregnant women with CH and/or previous PE and maternal and neonatal outcomes.

Materials and Methods

A randomized controlled trial (RCT) conducted between January 2008 and November 2011, in the Division of Obstetrics and in the Physical Therapy Outpatient Clinic of the Women's Hospital Professor Dr. José Aristodemo Pinotti (CAISM) of the University of Campinas (UNICAMP). Approval was obtained from the Research Ethics Committee of the Medical School of the University of Campinas (FCM-UNICAMP) (929/2007), registered on the website (www.clinicaltrials.gov), under number NCT01395342.

Sample size was calculated by using a comparison of prevalence rates of PE in women at higher risk of developing the disorder (16% to 18%) (26). Considering a lower prevalence of PE in high-risk pregnant women with no physical activity (PA) in 16% and with moderate-intensity PA and/or low-intensity PA in 1.6% and presuming a significance level of 5% and a power of 80%, sample size was estimated at n=58 participants for each group. Maintaining the same level of significance, the power of the test was calculated, based on the results found for the main variables: weight of the NB (80.3%) and Apgar score assigned at one minute (99%).

Eligible pregnant women according to preestablished criteria were selected in the prenatal outpatient clinic and invited to participate in the study.

One-hundred and sixteen pregnant women were randomized, diagnosed with CH, a history of PE in previous pregnancies or both, between 12 and 20 weeks of gestation and aged over 18 years. CH was defined as hypertension (BP $\geq$ 140/90 mmHg) diagnosed before pregnancy, or before completing 20 weeks of gestation. Previous preeclampsia was considered a reported history of hypertension and proteinuria after 20 weeks of gestation in previous pregnancies.

Women with multiple pregnancies, cervical insufficiency, vaginal bleeding, heart disease, systemic lupus erythematosus (SLE), kidney failure and neurologic disorders were excluded from the study. For inclusion in the study, pregnant women also could not be engaged in any supervised physical exercise, at the time of selection and when signing a free written informed consent term (WICT).

Pregnant women were randomized using an opaque sealed envelope that was sequentially numbered and statistically generated by a computer program, with allocation concealment (shielding the investigator). The envelope contained information about the random allocation group: a study group (SG), engaged in physical exercise with a stationary bicycle once a week under the supervision of a physical therapist, or a control group (CG), not engaged in any physical exercise. Random allocation of the subjects was performed by another investigator, who did not participate directly in the research study.

Pregnant women from the SG performed thirty minutes of physical exercise using a stationary bicycle (SB), a BM40000 Movement® horizontal bench professional model, under the supervision of the investigator, once a week after study inclusion (between 12 and 20 weeks of gestation), every week until the end of pregnancy.

The session began with adequate preparation of the pregnant woman for the performance of physical exercise. The woman was seated in a chair, where her shoes were removed and replaced by disposable protective foot covers. Subsequently, BP was measured and the watch and heart rate monitor waistband (POLAR® model CS300 multi) were positioned to record heart beats per minute (bpm). The watch was placed in the left wrist and the band was adapted to the inframammary region.

The seat of the SB was individually adapted for postural correction and height of the pedal according to weight, height and gestational week. As a result, the woman remained in a comfortable position and was maximally protected from possible joint damage. Pregnant women started to cycle and were instructed to try to maintain a HR 20% above resting values, not surpassing a value of 140 bpm (27) during the 30 minutes of exercise performance. Exercise intensity was gradually adjusted until the proposed parameters were reached. At approximately two minutes before the end of the exercise, the woman was instructed to decrease the speed of cycling, until the end of the established time. Stretching exercises were performed for five minutes following instructions, with the woman still on the bicycle, prioritizing the anterior and posterior chains of the lower limbs and relaxation of the lumbar spine. In the end, the woman was removed from the SB with the assistance of the physical therapist, seated for five minutes in a comfortable chair and waiting for the final BP measurement.

Exercise with a SB was performed in an adequate setting, with appropriate ventilation and illumination. Pregnant women were instructed to have a light meal about one hour before the performance of exercise and to wear comfortable clothes.

Pregnant women from the CG did not receive instructions on the practice of physical exercise and followed routine prenatal care.

Data related to sociodemographic and clinical characteristics (age, BMI, race, marital status, obstetrical data, history of CH and PE and the practice of previous physical exercise) were collected at the time the pregnant woman was included in the study. Data on delivery care and maternal outcome were gathered by consulting the computerized charts at CAISM. Data was retrieved from the medical charts by the researcher responsible and transcribed to a file specially designed for the collection of information. When the delivery did not take place in CAISM, additional contact was made by direct telephone call or personally to supplement possible information.

Maternal outcome evaluated were: hospitalization in the ICU and morbid conditions defined by the presence of any complications during pregnancy, at the time of delivery or postpartum period, such as PE, eclampsia, HELLP syndrome and others.

The neonatal outcome evaluated were: birth weight, adequacy of weight to gestational age (28), gestational age at the first trimester by ultrasound, Apgar at the first and fifth minutes, hospitalization in the ICU or semi-intensive neonatal care unit and neonatal morbidity (respiratory distress syndrome, intraventricular bleeding and others).

An intention to treat analysis was performed, without replacement values for missing data. Sociodemographic and clinical characteristics were evaluated by the chi-square tests or Fisher's exact test (for qualitative variables) and by the Student's t test or Mann-Whitney test (for quantitative variables), in addition to calculation of

relative risk (RR) and their respective 95% confidence intervals (CI). For neonatal outcomes, a COX multiple regression model technique was used to calculate the value of risk adjusted to Body Mass Index (BMI), race, number of pregnancies, CH and history of PE, and their respective 95%CI. SAS program version 9.2 was used for all analyses and the significance level assumed was 5%.

Results

Among the eligible pregnant women (n=152), 36 were excluded and 116 were randomized. Of the randomized women, 58 were allocated to each group. Three pregnant women from the SG and nine from the CG did not give birth in CAISM and data was retrieved from the charts of six of these women. One pregnant woman discontinued the study due to abortion, failing to perform any physical exercise session, since the event occurred soon after randomization (15 weeks of gestation). Fifty-six (56) women from the SG and 53 from the CG were analyzed for the variables type of delivery and maternal/fetal outcome (Figure 1).

The mean number of physical exercise sessions performed by the 58 pregnant women from the SG was 9.24 ± 7.03 . Of the women who performed few sessions (below the mean value of the group), 14 chose to interrupt the exercise, due to a change of city address/prenatal location or another personal reason that prevented them from adhering to exercise protocol.

No complications were observed during physical exercise sessions, e.g. difficult-to-control hypertension, hyperthermia, musculoskeletal lesions, or other complications identified that demanded interruption of the exercise.

The groups were considered homogeneous in all sociodemographic and clinical variables evaluated. Most pregnant women were white, obese, led a sedentary lifestyle, aged between 30 and 39 years and had a steady partner. Among the risk factors, 31 had PE in a previous pregnancy, 105 had CH and 20 had both conditions combined (Table 1).

There were no differences between the groups regarding mode of delivery, indication of cesarean section and maternal complications. In a similar manner, exercise did not represent a risk for these variables. Among the 77 pregnant women who had cesarean sections, 23 had more than one indication. The most frequent indications were maternal disease, repeat cesarean sections and fetal distress. The most prevalent maternal morbidity was PE. There was one patient with the HELLP syndrome and one with acute pulmonary edema (Table 2). Recurrence of PE (4.6%) was observed in two pregnant women from the SG and three from the CG (data not shown in the Tables).

There was one fetal death in the study due to difficult-to-control CH in a pregnant woman with a history of PE and chronic hypertension for three years. She was hospitalized in CAISM, at 26 weeks of gestation, for control of blood pressure and follow-up of fetal vitality, presenting severe fetal growth restriction (FGR), Doppler flow meter was altered in the umbilical artery and ductus venosus, both with reversed diastole. Three days after fetal demise was confirmed, fetal weight was 0.460 kg.

The majority of NB was of the male gender (55.5%). Mean gestational age was 38.2 ± 1.9 in the SG and 37.5 ± 2.2 in the CG ($p=0.09$) (data not shown in the Table). There were no differences in variables related to neonatal outcome and

neonatal risk was not shown to be increased (Table 3). Among the neonatal morbid conditions, the most prevalent was respiratory distress syndrome (10.6%), followed by early low serum glucose levels (7.45%).

After adjusted multiple regression analysis, physical exercise did not represent a risk for the neonatal outcomes studied: low birth weight (<2500g), macrosomy ($\geq$ 4000g), adequacy of weight and prematurity (<37 weeks of gestation) (Table 4).

Comment

The results of this study indicated that physical exercise with a SB in pregnant women with CH and/or previous PE did not determine the delivery method or interfere with maternal and perinatal results, not representing a risk for prematurity, low fetal weight or hypertensive complications.

This RCT was conducted in CAISM, a tertiary hospital, located in the city of Campinas, state of São Paulo, in the southeast of Brazil, referral center for complex obstetrical cases for the health units of neighboring cities. Pregnant women initiating prenatal care in these municipalities or in basic health units of the city of Campinas identified as having gestational risk are referred to specialized prenatal outpatient clinics (CAISM) for follow-up. This condition, added to the fact that most pregnant women previously led a sedentary lifestyle, could explain the great amount of women refusing to participate in the study and adhere to the systematized program for the performance of exercise or any other aerobic activity (29, 30). Many allegedly had difficulty in meeting the demands and proposals of the program, discontinuing after some sessions, missing many sessions, showing a low adherence to the protocol.

High cesarean section rates were observed in both groups (70.6%), numbers much higher than those reported in the international literature. Data published by the Ministry of Health in 2008, however, indicated a rate of 48.4% of cesarean section in Brazil, that surpassed the 50% range in the year 2011 (31). In the State of São Paulo, according to the State Data Analysis System Foundation (32), the rate of cesarean section was 58.7% in 2010, although the WHO recommends a rate of 15% as the optimal value (33).

The high rates of cesarean section found in this study could be related to the characteristics of sample selection. The pregnant women included represented a population at high gestational risk, because in addition to a risk for PE, they were chronically hypertensive and/or had a history of PE. Furthermore, the majority was obese at study inclusion, and 25 (23.5%) of these women were considered morbidly obese.

It is well-known that obesity is an important risk factor for operative delivery (34). In a metaanalysis including 33 studies, overweight, obese and morbidly obese pregnant women, had a twofold to threefold increased risk for cesarean section, when compared to pregnant women of normal weight. The risk increased proportionally to an increase in BMI in overweight (OR=1.46, 95%CI 1.34–1.60); obese (OR=2.05, 95%CI 1.86–2.27), and morbidly obese (OR=2.89, 95%CI 2.28–3.79) pregnant women (35).

Among the morbid maternal outcome, the most prevalent in this study was PE. However, it could be observed that physical exercise did not increase the rate of PE development, regardless of the number of exercise sessions, since the rate of women who did not have a morbid condition was 84.4%. These

results corroborated the findings by Yeo, et al (36) who studied pregnant women with a previous history of PE and also found no difference in PE development between those engaged in walking and those performing stretching exercises, five times a week during pregnancy.

In our study, the recurrence of PE was observed in five pregnant women (two from the SG and three from the CG), suggesting that physical activity with a SB once a week, did not interfere in PE development and may be considered safe for pregnant women with previous PE. It has been well-established that the recurrence of PE is associated with worse neonatal outcomes (37).

There is no consensus in the literature about an association between preterm delivery in low-risk pregnant women and physical (38-40) or occupational (18, 41, 42) activity during pregnancy. In the same manner, in our study there was no risk for prematurity in the SG. This corroborated a Cochrane review that also demonstrated a lack of association between aerobic exercise and prematurity in low-risk pregnant women (RR=1.82, 95%CI 0.35-9.57) (43). However, a study conducted in the South of the country (Brazil) demonstrated that leisure-time activity during pregnancy was associated with a lower risk of prematurity (44).

We found only one study on physical activity (walking vs. stretching) in pregnant women at risk with previous PE. That study demonstrated a prematurity rate of 22% among pregnant women who walked compared to 11% who only performed stretching exercises (insignificant difference) (35). An explanation for the different results obtained could be that the controls were distinct (stretching versus no intervention), as well as the intervention performed (walking versus SB). Furthermore, physical exercise sessions for our patients took place under

direct and continuous professional supervision, permitting better control of the intensity and uniformity of the programmed activity, promoting better results.

Low birth weight (<2500g) was not significant in the SG, compared to the CG. These results are similar to those in a study by Yeo et al (36) who also evaluated pregnant women at risk, in which no difference in newborn weight was observed among women who walked and stretched throughout pregnancy. However, other researchers observed that women who started moderate-intensity physical exercise in the first trimester (45, 46) or who worked (47) had infants with a higher birth weight and sedentary women had newborns with a higher weight at birth (42). Clapp et al (45) observed an increase in the velocity of placental growth and improvement in placental function which could be attributed to favorable physiological alterations due to physical exercise, such as an increase in maternal blood circulation.

In contrast, women performing high-intensity physical activity during pregnancy may have more low-weight and small for gestational age (SGA) newborns at birth (38, 48). These neonatal outcomes are also caused by the presence of CH, which is known to increase the risk of SGA and low Apgar scores at one and five minutes (5). In our study, no difference in adequacy of weight to gestational age was observed, as well as in Apgar scores, probably because exercise was of low intensity and controlled, therefore considered safe for fetal vitality.

A recent RCT evaluating the effect of aerobic exercise on sedentary pregnant women who danced or stretched during 60-minute periods, twice a week, and exercised 30 additional minutes at home in alternate days, showed better and higher 1-minute Apgar scores in the exercise group, without any significant difference at five minutes of life (17). It is well-known that a low Apgar score,

especially one that persists at five minutes, is indicative of higher neonatal mortality and morbidity (49, 50). In the present study, although Apgar scores showed no difference in both time periods measured, neonatal morbidity rate was equally elevated in both groups. This could be related to a greater presence of premature infants and low birth weight.

A possible skepticism about the design of this study was the fact that physical exercise was performed by morbidly obese women and those with chronic arterial hypertension, considered relative contraindications for the performance of these activities, according to the American College of Obstetrics and Gynecology (ACOG) (27). That is why low-intensity systematized physical exercise was performed only once a week after medical permission, under the direct and continuous supervision of a specialized trained physical therapist, in a hospital-based outpatient facility specialized in high complexity care of pregnant women. In case of any complication, additional support was readily available.

Women from the SG permitted the observation of the physiological effects of physical exercise performed during pregnancy on maternal well-being, in addition to establishing a closer link to healthcare professionals who participated in the prenatal care in weekly meetings. There was a greater commitment to maternal and fetal healthcare that was reflected in a better prenatal follow-up. It may be speculated that women who understood the importance of preventing PE and other complications of pregnancy were those that best adhered to the exercise program with a SB.

In conclusion, physical exercise using a SB in pregnant women with CH and/or previous PE, performed once a week under professional supervision, did not interfere in the delivery method and did not produce maternal and neonatal risk for

the occurrence of morbidity and hospitalization in the ICU. Women with CH and/or previous PE, even those leading a sedentary lifestyle before pregnancy, may initiate physical exercise with controlled intensity and adequate prescription. In future studies, it may be relevant to evaluate adhesion to physical exercise and lifestyle changes begun during the gestational period and the benefits of perpetuating this highly recommended behavior in these women. Since pregnancy determines individual and familial mobilization, it could represent a particularly opportune moment to initiate lifestyle changes in women with hypertensive disorders or at risk for this morbid condition.

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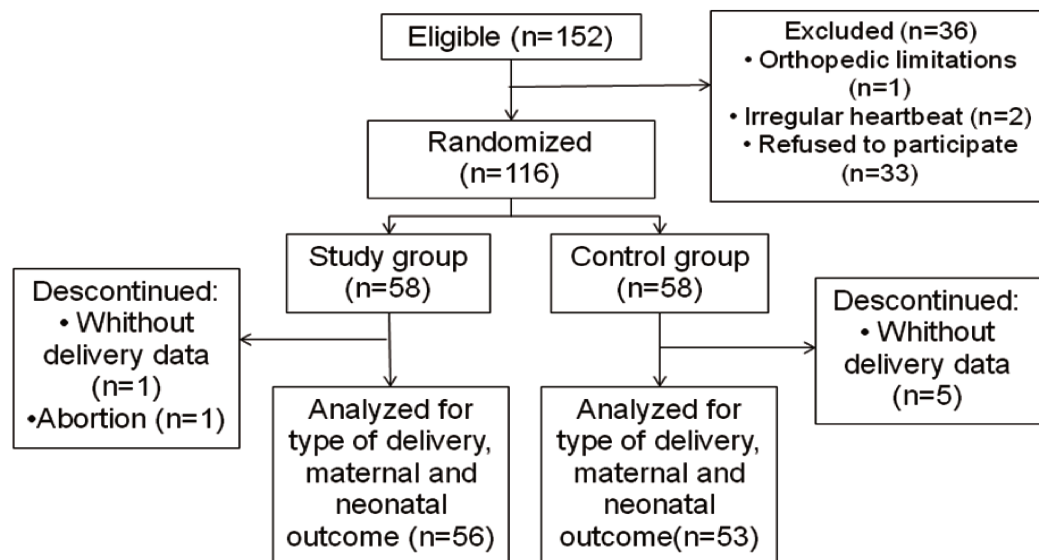


Figure 1. Flow chart of inclusion of pregnant in the study

Table 1 – Baseline characteristics of pregnant women with chronic hypertension and/or previous PE, according to exercise or non-exercise group

Variable	STUDY GROUP (n=58)	CONTROL GROUP (n=58)	P value ^a
Age(years), n(%)			.82 ^b
<19	1 (1.7)	1 (1.7)	
20-29	21 (36.2)	20 (34.5)	
30-39	27 (46.6)	31 (53.5)	
≥40	9 (15.5)	6 (10.3)	
BMC at inclusion, kg/m²			.57
18.5 a 24.9	4 (6.9)	6 (10.3)	
25 a 29.9	13 (22.4)	11 (19.0)	
30 a 39.9	26 (44.8)	31 (53.5)	
≥ 40	15 (25.9)	10 (17.2)	
Race/color, n(%)			.24
Non white	17 (29.3)	23 (39.7)	
Mean of gestational age at inclusion^d	17.3±3.4	18.5±3.4	.62 ^c
Parity, n(%)			.34
0	13 (22.4)	9 (15.5)	
≥1	45 (77.6)	49 (84.5)	
Previous abortion, n(%)	17 (29.3)	15 (25.9)	.67
Previous PE, n(%)	16 (27.6)	15 (25.9)	.83
CH, n(%)	51 (87.9)	54 (93.1)	.34
CH e previous PE, n(%)	9 (15.5)	11 (19.0)	.62
Marital status, n(%)			1.00 ^b
With a partner	53 (91.4)	54 (93.1)	
Physical exercise prior pregnancy, n(%)	6 (10.5)	4 (7.1)	.74 ^b

^a Calculated with chi-square test; ^b Calculated with the Fisher's exact test; ^c Calculated with t de Student; ^d Data are given as mean±SD. CH= chronic hypertension, BMI= body mass index, PE= preeclampsia

Table 2 – Type of delivery and maternal outcome in pregnant women with chronic hypertension and/or previous PE, according to exercise or non-exercise group

Outcome	STUDY GROUP (n=56)	CONTROL GROUP (n=53)	Relative Risk (95%CI)	P value ^a
Type of delivery, n(%)				.13
Vaginal delivery	20 (35.7)	12 (22.6)	Reference	
Cesarean	36 (64.3)	41 (77.4)	0.83 (0.65-1.06)	
Indication for cesarean, n(%)				
Repeat cesarean sections	8 (17.4)	13 (26.5)	0.62 (0.28-1.37)	.22
Fetal distress	8 (17.4)	10 (20.4)	0.80 (0.34-1.88)	.60
Maternal disease	12 (26.1)	13 (26.5)	0.92 (0.46-1.85)	.82
Cephalopelvic Disproportion/macrossomy	3 (6.5)	4 (8.2)	0.75 (0.18-3.20)	1.00 ^b
Failure to induce labor	8 (17.4)	3 (6.1)	2.67 (0.74-9.55)	.11
Other	7 (15.2)	6 (12.3)	1.17 (0.42-3.26)	.76
Maternal morbidity, n(%)				.89 ^b
No morbidity	48 (85.7)	44 (83)	Reference	
PE	7 (12.5)	8 (15.1)	0.86 (0.32-2.12)	
Other	1 (1.8)	1 (1.9)	0.92 (0.06-14.25)	
Maternal hospitalization in the Intensive Unit Care, n(%)	5 (9.1)	8 (15.1)	0.60 (0.21-1.72)	.33

^aCalculated with chi-square test; ^bCalculated with the Fisher's exact test; PE=preeclampsia

Table 3 – Neonatal outcome in pregnant women with chronic hypertension and/or previous PE, according to exercise or non-exercise group

Outcome ^d	STUDY GROUP n(%)	CONTROL GROUP n (%)	Relative Risk (95%CI)	P value ^a
Birth weight, g (n=108)				.55 ^b
< 2500	9 (16.4)	11 (20.7)	0.83 (0.38-1.84)	
2500 a 3999	41 (74.5)	40 (75.5)	Reference	
≥4000	5 (9.1)	2 (3.8)	2.28 (0.47-11.14)	
Neonatal adequacy of weight to gestational age (n=108)				.45
SGA	5 (9.1)	9 (17.0)	0.53 (0.19-1.46)	
AGA	41 (74.5)	35 (66.0)	Reference	
BGA	9 (16.4)	9 (17.0)	0.88 (0.38-2.02)	
Gestational age at birth, wk (n=108)				.10
<37	11 (20.0)	18 (34.0)	0.59 (0.31-1.13)	
≥37	44 (80.0)	35 (66.0)	Reference	
Apgar 1 minute (n=107)^c				.04
<7	10 (18.2)	3 (5.8)	3.15 (0.92-10.82)	
≥7	45 (81.8)	49 (94.2)	Reference	
Apgar 5 minutes (n=107)^c				.24 ^b
<7	3 (5.4)	0 (0.0)	Not calculated	
≥7	52 (94.5)	52 (100)		
Neonatal hospitalization in Intensive Unit Care, (n=107)^c				.82 ^b
Yes	12 (22.2)	13 (24.5)	0.91 (0.46-1.80)	
No	42 (77.8)	40 (75.5)	Reference	
Neonatal morbidity (n=100)^c				.40
Yes	16 (32.0)	20 (40.0)	0.80 (0.47-1.36)	
No	34 (68.0)	30 (60.0)	Reference	

^aCalculated with chi-square test; ^bCalculated with the Fisher's exact test, SGA= small for gestational age, ADA= adequate for gestational age, BGA= big for gestational age; ^cThe number of subjects changed due to lack of data to the variables; ^dExcluded one case of fetal death in second trimester

Table 4 – Multiple regression analysis adjusted with relative risk

Variable ^c	Relative Risk ajusted ^a (95%CI)
Birth weight, g	
< 2500	0.56 (0.26-1.25)
> 2500	Reference
Birth weight^b, g	
< 4000	Reference
> 4000	2.16 (0.41-11.37)
Neonatal adequacy of weight to gestational age	
SGA/ BGA	1.17 (0.73-1.87)
ADA	Reference
Gestational age at birth, wk	
<37	0.53 (0.26-1.06)
≥37	Reference

^aAdjusted for body mass index, race/color, number of gestation, chronic hypertension and previous preeclampsia; ^bIt was not possible to adjusted for chronic hypertension, SGA= small for gestational age, ADA= adequate for gestational age, BGA= big for gestational age; ^cExcluded one case of fetal death in second trimester

4. Discussão

A revisão sistemática indicou o efeito protetor da atividade física de lazer na prevenção da PE. No entanto, o ensaio controlado aleatorizado (ECA) sobre o exercício físico com bicicleta estacionária (BE) em gestantes de risco para PE, realizado sob supervisão profissional, não apresentou diferenças. Considerando que o ensaio clínico é o desenho metodológico ideal para avaliar uma intervenção e, a partir disso, verificar seus desfechos, o único estudo ECA incluído na revisão sistemática, semelhante a este, avaliou o exercício físico como forma de intervenção na gestação e também não observou diferença na incidência de PE entre os grupos. Neste estudo, a intervenção aparentemente não foi determinante e não influenciou o percurso natural do desenvolvimento da PE.

As repercussões maternas durante o parto são determinantes nas repercussões neonatais. Neste estudo, quando avaliadas as repercussões neonatais, as gestantes com HAC e/ou PE prévia que realizaram exercício físico com BE não apresentaram associação de risco para baixo peso ao nascer, macrossomia, prematuridade e morbidade neonatal. A literatura é controversa e não existe um consenso do real efeito do exercício físico com este impacto neonatal. Alguns relatam que gestantes que realizam exercício aumentam o

gasto energético, portanto o RN apresenta baixo peso ao nascer. Contudo, outros estudos analisam o efeito do exercício físico como melhora no sistema circulatório, aumentando o aporte nutricional do RN e, conseqüentemente, favorecendo o maior peso ao nascimento.

Quando se analisam os efeitos da atividade física e do exercício físico, diversos fatores devem ser considerados, como intensidade, frequência, duração e modalidade de exercício executado. Do mesmo modo, quando se avalia o exercício físico durante a gestação, outros fatores devem ser acrescentados para controle, como o período gestacional em que foram iniciados os exercícios, o condicionamento físico anterior da gestante, histórias de eventos gestacionais e obstétricos prévios, índice de massa corpórea, risco gestacional atual, dentre outros. Todos esses fatores, se não controlados adequadamente, podem repercutir isoladamente em desfechos maternos e perinatais distintos, funcionando como fatores confundidores.

Estes fatos podem explicar e justificar as dificuldades de se realizar a revisão sistemática sobre exercício físico e gestação. Devido às diferentes metodologias apresentadas e aos diversos países em que foram publicados, os resultados muitas vezes representam apenas as diferenças culturais entre os países. Essas diferenças podem ser observadas nas várias atividades de lazer reportadas em alguns estudos, como até mesmo equitação e jogos de golfe. Deve-se considerar que, em geral, nos países desenvolvidos, as mulheres com condição socioeconômica mais elevada e alto nível de escolaridade apresentam maior adesão às atividades físicas durante a gestação. Todavia, no presente

estudo, em outro contexto social, realizado na cidade de Campinas, onde a maioria das gestantes selecionadas vem de extrato mais pobre da população e apresenta estilo de vida sedentário, estas referiam não exercer atividade remunerada, justificando as altas taxas de gestantes que recusaram ou descontinuaram o exercício físico programado pela aleatorização.

Acredita-se ser necessário maior conscientização das mulheres sobre os benefícios do exercício físico durante a gestação para que as questões sociais envolvidas e que funcionam como vieses não desprezíveis possam ser transcendidas. Principalmente as gestantes de alto risco e que apresentam contraindicações relativas para a realização de exercício físico, de acordo com o Colégio Americano de Ginecologia e Obstetrícia, necessitam ser conscientizadas de que, quando o exercício é realizado de modo controlado, supervisionado por especialista, com escolha de modelo apropriado para sua condição e idade gestacional, poderá trazer benefícios de maneira segura ao binômio mãe-feto, como foi observado neste estudo.

O exercício físico já é descrito como padrão de tratamento para as desordens hipertensivas em pessoas não-gestantes, da mesma forma que já é consenso que o exercício durante a gestação de baixo risco melhora o estilo de vida e saúde maternas. Com isso, este estudo comprova que a gestante hipertensa que realiza exercício físico durante a gestação não apresenta aumento de risco para as morbidades maternas e neonatais.

Cumpram-se que as gestantes com HAC e/ou PE prévia que realizaram exercício físico durante a gestação apresentaram maior comprometimento com sua saúde, frequentando semanalmente o Hospital da Mulher (CAISM) para realizar exercício, facilitando o seu acesso ao médico, tirando dúvidas relacionadas à gestação com profissionais de saúde. Essas não apresentaram complicações maternas/perinatais e, através de sua vivência, apresentam ainda a possibilidade de manter o exercício físico após a gestação, mudar seu estilo de vida, e assim melhorar a hipertensão a longo prazo.

5. Conclusões

- A atividade física de lazer apresentou efeito protetor na prevenção da pré-eclâmpsia nos estudos de coorte e caso-controle, principalmente quando comparada à atividade ocupacional.
- Devido à heterogeneidade dos estudos analisados na revisão sistemática, não foi possível avaliar a intensidade ideal para garantir o efeito protetor do exercício físico.
- O exercício físico com bicicleta estacionária em gestantes com hipertensão arterial crônica e/ou pré-eclâmpsia prévia, no ensaio controlado aleatorizado, realizado sob supervisão de um profissional, uma vez por semana, não se associou à via de parto, repercussões maternas como morbidade, risco para a pré-eclâmpsia e internação materna na Unidade de Terapia Intensiva. Igualmente não apresentou associação com as repercussões neonatais, como peso ao nascer, idade gestacional, adequação do peso à idade gestacional, no índice de Apgar de primeiro e quinto minutos, morbidade neonatal e internação do recém-nascido na Unidade de Terapia Intensiva.

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7. Anexos

7.1. Anexo 1 – Lista de Verificação

Critérios	Incluída	Excluída
Hipertensão arterial crônica e/ou		
Pré-eclâmpsia em gestação anterior	() sim	() não
De 12 a 20 semanas gestacionais	() sim	() não
Gestação múltipla	() não	() sim
Cardiopata	() não	() sim
Incompetência istmo-cervical	() não	() sim
Lúpus eritematoso sistêmico (LES)	() não	() sim
Insuficiência renal	() não	() sim
Sangramento Persistente	() não	() sim
Apresentar doença neurológica	() não	() sim
Pode participar do estudo?	() sim	() não
Vai participar do estudo?	() sim	() não



Se a mulher preencher todos os itens em incluída anotar:

Nome: [_____]

HC: [_____]

Nº na pesquisa: [_____]

Grupo: [1] estudo [2] controle

7.2. Anexo 2 – Ficha de coleta de dados sociodemográficos e clínicos

AVALIAÇÃO DO EXERCÍCIO FÍSICO COM BICICLETA ESTACIONÁRIA EM GESTANTES COM RISCO PARA O DESENVOLVIMENTO DA PRÉ-ECLÂMPsia

Número na pesquisa: ____|____

Data: ____/____/____

1. Grupo: [1] Estudo [2] Controle

Dados Pessoais:

2. Data de nascimento: ____/____/____ 3. Idade ____|____|

4. Raça/Cor: [1] Branca
[2] Preta
[3] Parda
[4] Amarela
[5] Indígena

5. Estado marital: [1] Com companheiro [2] Sem companheiro

6. Peso: ____|____|, ____|____| kg 8. IMC: ____|____|

7. Altura: ____|____| metros

9. Hipertensão arterial crônica: [1] Sim [2] Não

10. Prática de exercício físico: [1] Sim [2] Não

11. Qual exercício: [1] Ginástica
[2] Musculação
[3] Natação
[4] Hidroginástica
[5] Jogos competitivos
[6] Outros. Qual? _____

12. Quantas vezes por semana: [1] Menos de uma vez
[2] Uma vez
[3] Duas vezes
[4] Três vezes
[5] Mais de três vezes

Dados Obstétricos:

13. Idade gestacional: ____|____|, ____|____| semanas

11. História obstétrica:

- a. Número de gestações anteriores: ____|____|
- b. Número de partos: ____|____| → **Em caso de nulíparas encerre aqui(00)**
- c. Número de abortos: ____|____|
- d. Quantos partos foram normais: ____|____|
- e. Quantos partos foram cesáreas: ____|____|

12. Número de gestações anteriores com pré-eclâmpsia: ____|____|

----- ✂ -----

Número na pesquisa: ____|____|

Nome: _____

HC: _____ Telefones: _____

7.3. Anexo 3 – Termo de Consentimento Livre e Esclarecido (TCLE)

Nº |__|__|

AVALIAÇÃO DO EXERCÍCIO FÍSICO COM BICICLETA ESTACIONÁRIA EM GESTANTES COM RISCO PARA O DESENVOLVIMENTO DA PRÉ-ECLÂPSIA

Responsável pelo projeto: Camila Schneider Gannuny

Nome: _____
RG: _____ Idade: _____ HC: _____
Endereço: _____
Bairro: _____ Cidade: _____
Telefone: () _____

Eu, _____, fui informada que:

Esta é uma pesquisa para ver se o exercício físico com bicicleta estacionária, de intensidade leve e moderada, previne o aparecimento da pré-eclâmpsia (pressão alta e alto nível de proteína na urina) em gestantes com maior risco para desenvolvê-la.

Sei que ao aceitar participar deste estudo receberei um envelope opaco e selado contendo um número e posso ser sorteada para ser incluída no grupo que vai (grupo estudo) ou no que não vai (grupo controle) realizar o exercício físico com bicicleta estacionária horizontal, sob supervisão, uma vez por semana durante trinta minutos no Ambulatório de Fisioterapia do Hospital da Mulher Professor Doutor José Aristodemo Pinotti - CAISM/UNICAMP, independente da minha vontade. Fui informada também, que seja qual for o grupo em que for incluída necessitarei comparecer uma vez por semana para avaliações regulares dos valores da pressão arterial e frequência cardíaca, além de ter que preencher a um questionário de qualidade de vida em três momentos diferentes.

Até o momento não foi observado nenhum risco para a mãe e para o bebê na realização dos exercícios físicos com bicicleta estacionária sob orientação.

Também fui informada que o atendimento pré-natal não vai ser alterado caso não aceite ou desista de participar do estudo. Qualquer dúvida sobre a pesquisa poderá perguntar à pesquisadora responsável, em qualquer momento. Poderei deixar de participar do estudo em qualquer momento, sem que isso prejudique o meu atendimento ou o do bebê após o parto. Meu nome e meus dados pessoais não serão divulgados, mesmo que os resultados sejam publicados em revistas ou apresentados em congressos. Toda documentação desta pesquisa será guardada por cinco anos após o término do estudo.

Se achar necessário pode entrar em contato com o Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP, pelo telefone: (19) 3521-8936 ou no ambulatório de Fisioterapia do CAISM/Unicamp com a pesquisadora responsável (Camila Schneider Gannuny/ Karina Tamy Kasawara) pelo telefone: (19) 3521-9428 ambos em horário comercial.

Concordo em participar voluntariamente do estudo.

Campinas, ____ de _____ de 20____.

Assinatura da participante

Pesquisadora responsável: Camila Schneider Gannuny/ Karina Tamy Kasawara

7.4. Anexo 4 – Ficha de coleta de dados do parto, repercussões maternas e perinatais

Data da coleta da informação: ____/____/____ Número na pesquisa: |____|____|____|

1. Grupo: [1] Estudo [2] Controle

DADOS DO PARTO

2. Data do parto: ____/____/____

3. Tipo de parto: [1] vaginal [2] vaginal com fórceps [3] cirúrgico

4. Início do trabalho de parto: [1] Espontâneo [2] Induzido [9] Não consta

5. Indicação da via de parto alta: [1] Iteratividade [2] Sofrimento fetal
[3] Desproporção céfalo-pélvico (DCP) [4] Patologia materna
[5] Não consta [6] Apresentação pélvica [7] Distócia funcional
[8] Outros _____ [9] Falha na indução [10] Macrosomia fetal

6. Episiotomia: [1] Sim [2] Não [3] Não consta

7. Anestesia: [1] Não houve [2] Raquianestesia [3] Peridural
[4] Bloqueio Pudendo/Local [5] Geral
[6] Combinada (Raqui+Peri) [7] Não consta
[8] Outros. _____

8. Momento de indicação da anestesia: |____|____| cm de dilatação

DADOS MATERNOS

9. Morbidade: [1] Não houve [2] Pré-eclâmpsia leve [3] Pré-eclâmpsia moderada
[4] Pré-eclâmpsia grave [5] Eclâmpsia [6] HELLP síndrome
[7] Sepses [8] Choque hemorrágico [9] Hemotransfusão
[10] Morte [11] Não consta [12] Outros. _____

10. Esteve internada na UTI: [1] Sim [2] Não [3] Não consta

DADOS DO RECÉM-NASCIDO (RN)

11. Óbito perinatal: [1] Sim [2] Não

12. Sexo do RN: [1] Feminino [2] Masculino [3] Indeterminado [4] Não consta

13. Peso do RN: |____|,|____|____| kg

14. Adequação do peso à idade gestacional: [1] PIG [2] AIG [3] GIG

15. Altura do RN: |____|____|,|____|____| cm

16. Ecografia: |____|____|+|____| semanas

17. CAPURRO: |____|____|+|____| semanas

18. APGAR 1º minuto |____|____| 19. APGAR 5º minuto |____|____|

20. RN permaneceu internado na UTI: [1] Sim [2] Não [3] Não consta

21. Morbidade neonatal: [1] SDR [2] Displasia Broncopulmonar
[3] Refluxo gastroesofágico [4] Hemorragia Perintraventricular (HPIV)
[5] Leucomalácia [6] Encefalopatia [7] Enterocolite
[8] Retinopatia da prematuridade [9] Não consta
[10] Outros. _____

Número na pesquisa: |____|____|____| HC: _____

Telefones: _____

Nome: _____

7.5. Anexo 5 – Carta de Aprovação do CEP

FACULDADE DE CIÊNCIAS MÉDICAS
COMITÊ DE ÉTICA EM PESQUISA

www.fcm.unicamp.br/pesquisa/etica/index.html

CEP, 18/12/07.
(Grupo III)

PARECER CEP: Nº 929/2007 (Este nº deve ser citado nas correspondências referente a este projeto)
CAAE: 0678.0.146.000-07

I - IDENTIFICAÇÃO:

PROJETO: “AVALIAÇÃO DO EXERCÍCIO FÍSICO COM BICICLETA ESTACIONÁRIA EM GESTANTES COM RISCO PARA O DESENVOLVIMENTO DA PRÉ-ECLÂMPsia”.

PESQUISADOR RESPONSÁVEL: Camila Schneider Ganunny

INSTITUIÇÃO: CAISM/UNICAMP

APRESENTAÇÃO AO CEP: 04/12/2007

APRESENTAR RELATÓRIO EM: 18/12/08 (O formulário encontra-se no *site* acima)

II - OBJETIVOS

Avaliar a eficácia do exercício físico com bicicleta estacionária na prevenção da pré-eclâmpsia em gestantes com hipertensão arterial crônica, pré-eclâmpsia em gestações anteriores, ou os dois fatores anteriores associados.

III - SUMÁRIO

O estudo será ensaio clínico aberto, controlado e aleatorizado por intenção de tratamento, composto por dois grupos de gestantes selecionadas no ambulatório de pré-natal do Centro de Atenção Integral à Saúde da Mulher (CAISM) na Universidade Estadual de Campinas (UNICAMP): no grupo estudo as gestantes realizarão exercícios físicos com bicicleta estacionária uma vez por semana sob supervisão de um fisioterapeuta, no Ambulatório de Fisioterapia do CAISM/UNICAMP, e o grupo controle seguirá a rotina de assistência pré-natal do CAISM/UNICAMP. Análise dos dados: as informações serão codificadas e duplamente digitadas, utilizando o software Epi Info, e para comparação da significância dos dados serão utilizados os testes T de Student e qui quadrado para avaliar a associação entre o exercício físico em bicicleta estacionária e a pressão arterial, e também a razão de risco para o respectivo IC95% entre os grupos.

IV - COMENTÁRIOS DOS RELATORES

O projeto apresenta-se bem redigido, com metodologia adequada. Os critérios de inclusão, exclusão e descontinuação dos sujeitos estão bem definidos; cálculo do tamanho amostral e análise estatística muito bem embasados por cálculos estatísticos. Os aspectos éticos e o Termo de Consentimento Livre e Esclarecido estão adequados às recomendações. O orçamento é detalhado e prevê ressarcimento de custos com alimentação para as voluntárias.

Devido à ausência de estudos que avaliem a eficácia do exercício físico com bicicleta estacionária orientado, na prevenção do aparecimento de pré-eclâmpsia em mulheres grávidas

com risco para desenvolvê-la, há necessidade da realização do mesmo. Além disso, nos serviços de saúde o exercício físico poderá ter um papel significativo para diminuição dos custos medicamentosos e possíveis internações advindas do desenvolvimento da pré-eclâmpsia.

As gestantes podem se beneficiar desse recurso como uma prática eficaz que melhora a qualidade de vida no período gestacional. Consideramos o projeto claro, objetivo, portanto preenche os requisitos necessários para aprovação.

Recomendação: Rever a frequência semanal com que será feito o exercício.

V - PARECER DO CEP

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP, após acatar os pareceres dos membros-relatores previamente designados para o presente caso e atendendo todos os dispositivos das Resoluções 196/96 e complementares, resolve aprovar sem restrições o Protocolo de Pesquisa, assim como todos os anexos incluídos na Pesquisa supracitada.

O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

VI - INFORMAÇÕES COMPLEMENTARES

O sujeito da pesquisa tem a liberdade de recusar-se a participar ou de retirar seu consentimento em qualquer fase da pesquisa, sem penalização alguma e sem prejuízo ao seu cuidado (Res. CNS 196/96 – Item IV.1.f) e deve receber uma cópia do Termo de Consentimento Livre e Esclarecido, na íntegra, por ele assinado (Item IV.2.d).

Pesquisador deve desenvolver a pesquisa conforme delineada no protocolo aprovado e descontinuar o estudo somente após análise das razões da descontinuidade pelo CEP que o aprovou (Res. CNS Item III.1.z), exceto quando perceber risco ou dano não previsto ao sujeito participante ou quando constatar a superioridade do regime oferecido a um dos grupos de pesquisa (Item V.3.).

O CEP deve ser informado de todos os efeitos adversos ou fatos relevantes que alterem o curso normal do estudo (Res. CNS Item V.4.). É papel do pesquisador assegurar medidas imediatas adequadas frente a evento adverso grave ocorrido (mesmo que tenha sido em outro centro) e enviar notificação ao CEP e à Agência Nacional de Vigilância Sanitária – ANVISA – junto com seu posicionamento.

Eventuais modificações ou emendas ao protocolo devem ser apresentadas ao CEP de forma clara e sucinta, identificando a parte do protocolo a ser modificada e suas justificativas. Em caso de projeto do Grupo I ou II apresentados anteriormente à ANVISA, o pesquisador ou patrocinador deve enviá-las também à mesma junto com o parecer aprovatório do CEP, para serem juntadas ao protocolo inicial (Res. 251/97, Item III.2.e)

Relatórios parciais e final devem ser apresentados ao CEP, de acordo com os prazos estabelecidos na Resolução CNS-MS 196/96.

VII - DATA DA REUNIÃO

Homologado na XII Reunião Ordinária do CEP/FCM, em 18 de dezembro de 2007.


Prof. Dra. Carmen Silvia Bertuzzo
PRESIDENTE DO COMITÊ DE ÉTICA EM PESQUISA
FCM / UNICAMP

7.6. Anexo 6 – Carta de Aprovação do CEP referente ao adendo



**FACULDADE DE CIÊNCIAS MÉDICAS
COMITÊ DE ÉTICA EM PESQUISA**

www.fcm.unicamp.br/pesquisa/etica/index.html

CEP, 22/02/11.
(PARECER CEP: N° 929/2007)

PARECER

I – IDENTIFICAÇÃO:

**PROJETO: “AVALIAÇÃO DO EXERCÍCIO FÍSICO COM BICICLETA
ESTACIONÁRIA EM GESTANTES COM RISCO PARA O DESENVOLVIMENTO
DA PRÉ-ECLÂMPsia”.**

PESQUISADOR RESPONSÁVEL: Camila Schneider Ganunny

II – PARECER DO CEP.

O Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas da UNICAMP tomou ciência e aprovou a inclusão da aluna de mestrado Karina Tamy Kasawara, referente ao protocolo de pesquisa supracitado.

O conteúdo e as conclusões aqui apresentados são de responsabilidade exclusiva do CEP/FCM/UNICAMP e não representam a opinião da Universidade Estadual de Campinas nem a comprometem.

III – DATA DA REUNIÃO.

Homologado na II Reunião Ordinária do CEP/FCM, em 22 de fevereiro de 2011.


Prof. Dr. Carlos Eduardo Steiner
PRESIDENTE do COMITÊ DE ÉTICA EM PESQUISA
FCM / UNICAMP