

Pain tolerance and cardiorespiratory fitness in women with dysmenorrhea

Tolerância à dor e aptidão cardiorrespiratória em mulheres com dismenorreia

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ABSTRACT

BACKGROUND AND OBJECTIVES: Hormonal changes are known to affect quality of life of women and may interfere in pain tolerance and cardiorespiratory exercise performance. Thus, the aim of this study was to evaluate and compare pressure pain tolerance threshold and cardiorespiratory fitness in women in luteal and follicular phases of the menstrual cycle.

METHODS: University students aged 18-30 years old with a regular menstrual cycle were evaluated for cardiorespiratory fitness (ergospirometry), pain perception through the visual analog scale and pressure pain tolerance (algometry).

RESULTS: When evaluated in follicular phase, the 13 participants exhibited a significant increase ($p<0.001$) in pain perception. Follicular phase also resulted in a significant reduction in pressure pain tolerance in all sites evaluated ($p<0.05$). At rest, follicular phase resulted in a significant increase ($p<0.05$) in systolic and diastolic blood pressure, but no effect was observed in heart rate. At peak exercise, follicular phase caused a significant reduction ($p<0.05$) in heart rate and peak VO₂, without significantly affecting speed, test duration and indicators of metabolism efficiency.

CONCLUSION: Healthy women with dysmenorrhea show higher pain perception in follicular phase, which results in increased pain sensitivity and prejudice in hemodynamic aspects at rest and during exercise, as well as in cardiorespiratory fitness, without significant alterations in metabolism.

Keywords: Dysmenorrhea, Menstrual cycle, Pain threshold, Physical fitness.

RESUMO

JUSTIFICATIVA E OBJETIVOS: As mudanças hormonais afetam a qualidade de vida das mulheres e podem interferir na tolerância à dor e no desempenho cardiorrespiratório. Assim, o objetivo deste estudo foi avaliar e comparar o limite de tolerância de dor à pressão e a aptidão cardiorrespiratória em mulheres nas fases lútea e folicular do ciclo menstrual.

MÉTODOS: Estudantes universitárias de 18 a 30 anos de idade com ciclo menstrual regular foram avaliadas quanto à aptidão cardiorrespiratória (ergoespirometria), percepção de dor pela escala analógica visual e tolerância de dor à pressão (algometria).

RESULTADOS: Quando avaliadas na fase folicular, as 13 participantes apresentaram aumento significativo ($p<0,001$) na percepção da dor. A fase folicular também resultou em uma redução significativa na tolerância de dor à pressão em todos os locais avaliados ($p<0,05$). Em repouso, a fase folicular resultou em um aumento significativo ($p<0,05$) na pressão arterial sistólica e diastólica, mas nenhum efeito foi observado na frequência cardíaca. No pico de exercício, a fase folicular causou uma redução significativa ($p<0,05$) na frequência cardíaca e no VO₂ máximo, sem afetar a velocidade, a duração do teste e os indicadores de eficiência do metabolismo.

CONCLUSÃO: Mulheres saudáveis com dismenorreia apresentam maior percepção de dor na fase folicular, o que resulta em aumento da sensibilidade à dor e prejuízo em aspectos hemodinâmicos em repouso e durante o exercício, bem como na aptidão cardiorrespiratória, sem alterações significantes no metabolismo.

Descritores: Aptidão física, Ciclo menstrual, Dismenorreia, Limiar de dor.

INTRODUCTION

During most part of life, women deal with hormonal cycles that generally occur at every 28 days, from menarche to menopause, regulated by the pituitary gland and ovaries through gonadotropic secretions¹. These hormones affect psychological aspects, as well as musculoskeletal sensitivity and quality of life of women².

A regular menstrual cycle can be divided into three consecutive phases: follicular (which starts on the first day of menstruation), ovulatory (which can last up to 3 days), and luteal (from the end of ovulation to the beginning of a new menstrual flow). There are reports of clinical conditions related to these phases, such as insulin resistance, supraventricular tachycardia, Raynaud syndrome, sleeping disorders and migraine³.

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Although regular exercise has been reported to reduce dysmenorrhea and physical and psychological symptoms⁴, changes in cardiorespiratory fitness and function may also occur, most likely in response to changes in body temperature and metabolism, accompanying hormonal curves and influencing aerobic performance and muscle strength^{3,5}. Regarding cardiorespiratory fitness, due to the growing rate of estrogen and higher secretion of noradrenalin in luteal phase, a significant improvement in exercise performance might be observed. However, in premenstrual stage performance exhibits a noticeable reduction related to the increase in progesterone levels⁶.

Chantler, Mitchell and Fuller⁷, found a significant reduction in time of treadmill test and in heart rate of women with dysmenorrhea exercising at follicular phase. Furthermore, there are also studies that could not identify any changes in flexibility, muscle strength, endurance, aerobic performance and reaction time over the menstrual cycle^{1,8,9}. These controversies justify the expansion of information about cardiorespiratory fitness along the menstrual cycle, especially with regard to determinants of cardiorespiratory performance: maximal oxygen uptake (VO_2 max), ventilation (VE), ventilatory equivalent of oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2), anaerobic threshold (AT) and respiratory compensation point (RCP). To the best of our knowledge no study so far has explored this issue.

When it comes to pain, it is more pronounced when estrogen levels fall¹⁰. However, a recent review⁶ points out that most recent studies show no changes in sensitivity to pain during the phases of the menstrual cycle, yet the authors report that, as there is still no consensus on the influence of the cycle on the sensation of pain in healthy women, more studies on this topic are necessary.

Therefore, the aim of this study was to evaluate and compare pressure pain tolerance threshold and cardiorespiratory fitness in women with dysmenorrhea in luteal and follicular phases of the menstrual cycle.

METHODS

This transversal observational study, female university health students (nursing, physical therapy, nutrition and physical education) were recruited through public announcement in the classrooms of health courses at a private university in the city of São Paulo (Brazil). The ones who agreed to participate (n=21) were invited to attend at the Laboratory of Exercise Physiology, where more instructions about the research protocol were provided. Inclusion criteria were ageing between 18 to 30 years old, having a regular menstrual cycle (between 28 and 32 days)³ and dysmenorrhea complaint. Students in use of hormonal contraceptives were excluded from the study, as well as current smokers, the ones who were in use of analgesic drugs, pregnant women or the ones who had already had babies, the ones with a history of uterine diseases and the ones who presented motor disabilities or did not perform one or more tests.

After receiving instructions on the research procedures, participants gave informed written participation consent, according to Declaration of Helsinki and Resolution 466/12 from the Brazilian Health Council.

Participants were assessed for anthropometry and body composition at their first visit to the Exercise Physiology Laboratory, where all study evaluations occurred. Height was measured with an appropriate stadiometer, and body weight was assessed in a digital scale with minimum possible clothes. Body composition was assessed by tetrapolar bioelectrical impedance, after 10 minutes of rest. The data collection team was composed by an exercise physiologist and a physical therapist.

All further assessments were conducted in two specific moments of the menstrual cycle^{1,3}: premenstrual or luteal phase (10 to 15 days before menstruation) and menstrual or follicular phase (between the first and third day of menstruation).

Pain perception

Data regarding pain intensity were collected by the visual analog scale (VAS). VAS consists of a straight line of 10cm that has "zero" (no pain) in one extremity, and "10" (maximal pain) in the other. Every participant was asked to mark a cross on the line indicating her discomfort level. The closest to zero, the less the level of perceived pain, and the closest to 10, the worse perceived pain was.

Pressure pain tolerance threshold (PPT) corresponds to the amount of pressure an individual can tolerate in a given site, measured in pounds by algometry (JTech Medical, Salt Lake City, UT, USA). Reliability of this test has already been demonstrated¹¹. Pressure was applied at a 90° angle (between the stimulation surface and the stimulated point) with a constant speed of 1kg/s. Volunteers were evaluated by the same examiner and equipment. The test was interrupted once the volunteer indicated the onset of pain, and the final amount of force applied was recorded. PPT was assessed bilaterally at the muscles vastus medialis, vastus lateralis, gluteus maximus, gluteus medius, iliopsoas, tibialis anterior, lumbar paraspinals, lumbar quadratus, pectoralis major and trapezius, as well as at the supraspinous ligaments between L4-S1^{12,13}.

Cardiorespiratory fitness was assessed by a ramp protocol in a breath-by-breath gas analysis system (Cortex Biophysik Metalyzer 3B, Stationary CPX System, Leipzig, Germany). The test was conducted in a treadmill with adjustable incline and speed (Albatroz VT2500, Vitality, São Paulo, Brazil). Data were collected and analyzed by a specific software (Cortex Biophysik Meta Soft CPX testing software, Leipzig, Germany).

Before testing, volunteers had their resting heart rate and blood pressure assessed, after 15 minutes of rest, with a heart rate monitor and a calibrated sphygmomanometer, respectively.

All participants were familiarized with the exercise of walking/running on a treadmill to determine the maximum comfortable cadence before testing. The actual test started with a speed of 3km/h and was increased by 0.5km/h at every 30 seconds, so that after 3 minutes test speed was reached. After that, the progressive ramp protocol began, with increasing incline of 1% at every 60s until the voluntary requested interruption (between 8 and 12 minutes).

The effort was considered maximal when three of the five following criteria were reached¹⁴: 1) heart rate (HR) equal to or higher than 95% of maximum predicted heart rate, 2) ventila-

tion exceeding 60% of maximum predicted voluntary ventilation (MVV), 3) respiratory quotient (RQ) equal to or higher than 1.10, 4) evidence of respiratory compensation point, and 5) presence of plateau of oxygen consumption (VO_2), i.e., increased effort without subsequent increase in VO_2 .

After testing, the participant walked at a speed that allowed her HR to reach 120 bpm or less. Maximal predicted heart rate for age was calculated as follows: $208 - 0.7 \times \text{age}^{15}$. Forced expiratory volume in the first second (FEV_1) was calculated by the following equation¹⁶: FEV_1 (liters) = $0.0309 \times \text{height (cm)} - 0.0201 \times \text{age (years)} - 1,405$. The expected MVV was calculated as follows¹⁶: $37.5 \times \text{FEV}_1 + 15.8$.

Ventilatory and metabolic parameters (VO_2 , HR and RQ)^{14,17,18} were determined at AT, RCP and at the highest VO_2 observed in the last 30 seconds of exercise (peak VO_2). Ventilatory equivalent of oxygen (VE/VO_2) and carbon dioxide (VE/VCO_2), as well as oxygen pulse were determined only at peak VO_2 . The respiratory exchange ratio (RER) represents the relationship between VCO_2 and VO_2 ¹⁴, and oxygen pulse (O_2 pulse) is the relationship between VO_2 and HR¹⁹. VE/VO_2 and VE/VCO_2 are ventilatory efficiency indicators and O_2 pulse is an indicative of left ventricular ejection. This study was approved by the local Ethics Committee (CAAE 43429215.9.0000.5377)

Data analysis

Data were analyzed using the statistical package GraphPad Prism version 6.0 for Windows (www.graphpad.com). Results were expressed as means \pm standard deviations. Comparisons between luteal and follicular phases were performed by Student's *t* test. The established significance level was 5% ($p < 0.05$).

RESULTS

Out of the 21 women initially enrolled in the study, 8 were excluded from the sample for not attending the assessments or for taking analgesic drugs. Thus, the final sample of this study was composed by 13 women with dysmenorrhea complaint. Most of them (77%) presented adequate BMI, but less than half (46%) exhibited adequate adiposity. Body water content and angle of phase were adequate in 92% of them (between 41% and 60% and between 5.3° and 10° , respectively), as shown in table 1.

Results of pain perception and pressure pain tolerance (algometry) are described in table 2. When evaluated in follicular phase, participants exhibited a significant increase ($p < 0.001$) in pain perception (assessed by VAS), and correlation between VAS in luteal and follicular phases showed moderate association ($r = 0.58$, $p < 0.001$). Also, follicular phase resulted in a significant reduction in pressure pain tolerance in all sites evaluated, indicating increase in pain sensitivity ($p < 0.05$).

The impact of follicular phase on several metabolic and cardiorespiratory parameters is shown in table 3. At rest, follicular phase resulted in a significant increase ($p < 0.05$) of 8mmHg in systolic and diastolic blood pressure (BP), but no effect was observed in HR.

No effects in ergospirometry parameters evaluated at AT (first ventilatory threshold) were observed in follicular phase when compared to luteal phase. Nonetheless, at RCP (second ventila-

tory threshold), parameters occurred sooner at follicular phase, but statistical significance was observed only in VO_2 and VO_2 relative to predicted values ($p < 0.05$).

Finally, at peak exercise, follicular phase caused a significant reduction ($p < 0.05$) in HR (4%), in HR relative to predicted (3 percentage points), peak VO_2 (13%) and VO_2 relative to predicted (8 percentage points), without significantly affecting speed, test duration, RQ and the indicators of ventilatory efficiency (VE/VO_2 e VE/VCO_2).

Table 1. General characteristics of the sample (n=13)

Variables	Mean \pm SD	n (%)
Age (years)	21.1 \pm 1.2	
Height (cm)	161.0 \pm 7.2	
Weight (kg)	60.9 \pm 13.1	
BMI (kg/m ²)	23.4 \pm 4.0	
Adequate BMI		10 (77)
%F	26.4 \pm 5.3	
Adequate %F		6 (46)
LM (kg)	44.4 \pm 7.3	
Relative LM (%)	73.5 \pm 5.4	
Adequate relative LM		1 (8)
Phase angle (degrees)	7.0 \pm 1.4	
Adequate phase angle		12 (92)
Body H ₂ O content (%)	54.2 \pm 4.8	
LM H ₂ O (%)	73.7 \pm 2.4	

SD = standard deviation; cm = centimeters; kg = kilograms; m² = square meters; BMI: body mass index; %F = percent body fat; LM = lean mass; H₂O = water.

Table 2. Pressure pain tolerance threshold in muscles and ligaments evaluated (n=13)

	Luteal phase	Follicular phase
VAS (cm)	1.2 \pm 1.3	6.6 \pm 1.8***
R Vastus medialis (lb)	7.7 \pm 2.6	5.9 \pm 1.8*
L Vastus medialis (lb)	8.5 \pm 2.1	5.8 \pm 1.8*
R Pectoralis major (lb)	4.6 \pm 1.1	3.2 \pm 1.4**
L Pectoralis major (lb)	4.7 \pm 1.3	3.3 \pm 1.2***
R Gluteus maximus (lb)	8.9 \pm 2.5	5.6 \pm 3.1***
L Gluteus maximus (lb)	9.2 \pm 3.2	6.2 \pm 2.2***
R Gluteus medius (lb)	7.1 \pm 1.7	4.9 \pm 1.5***
L Gluteus medius (lb)	7.9 \pm 2.8	5.6 \pm 2.7***
R Iliopsoas (lb)	8.4 \pm 2.1	4.9 \pm 1.6***
L Iliopsoas (lb)	7.3 \pm 2.0	5.3 \pm 1.6*
R Lumbar paraspinals (lb)	8.1 \pm 2.8	5.6 \pm 2.6**
L Lumbar paraspinals (lb)	7.9 \pm 2.8	5.4 \pm 2.7*
R Trapezius (lb)	5.1 \pm 1.6	3.8 \pm 1.5*
L Trapezius (lb)	4.9 \pm 1.6	3.4 \pm 1.4**
Supraspinous ligament L4-L5 (lb)	7.4 \pm 1.3	5.5 \pm 2.2**
Supraspinous ligament L5-S1 (lb)	7.6 \pm 2.7	5.3 \pm 2.2**

Data expressed as means \pm standard deviations. VAS = visual analog scale; cm = centimeters; R = right; L = left; lb = pounds. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 3. Hemodynamic, ergospirometry and metabolic parameters of women in luteal and follicular phases of the menstrual cycle

	Luteal phase	Follicular phase
Rest		
HR (bpm)	79±15	84±10
Systolic BP (mmHg)	112±11	120±13*
Diastolic BP (mmHg)	69±7	77±10*
Anaerobic Threshold		
HR (bpm)	114±14	115±11
FC (% of peak)	61±6	64±5
VO ₂ (mL/kg/min)	14.3±2.6	13.8±3.5
VO ₂ (% of peak)	44±8	49±12
RQ	0.75±0.04	0.75±0.06
Respiratory compensation point		
HR (bpm)	176±11	165±15
HR (% of peak)	95±5	92±5
VO ₂ (mL/kg/min)	30.4±4.6	25.1±5.1**
VO ₂ (% of peak)	92±5	87±6**
RQ	1.04±0.06	1.01±0.07
Peak exercise		
Maximal age predicted HR (bpm)	193±1	
Peak HR (bpm)	186±9	179±14*
Peak HR (% predicted)	96±6	93±7*
Predicted VO ₂ max (mL/kg/min)	52.3±0.5	
Peak VO ₂ (mL/kg/min)	32.9±4.4	28.7±4.7*
Peak VO ₂ (% predicted)	63±8	55±9*
Peak RQ	1.11±0.06	1.08±0.08
Peak VE/VO ₂	34.8±5.0	34.7±5.5
Peak VE/VCO ₂	32.0±3.3	32.9±3.4
Testing speed (km/h)	5.8±0.7	5.8±0.7
Test duration (minutes)	10.1±2.0	9.4±2.2

Data expressed as means ± standard deviations. HR = heart rate; bpm = beats per minute; BP = blood pressure; mmHg = millimeters of mercury; VO₂ max = maximal oxygen consumption; mL/kg/min = milliliters per kilogram per minute; % = percent; RQ = respiratory quotient; VE/VO₂ = ventilatory equivalent of oxygen; VE/VCO₂ = ventilatory equivalent of carbon dioxide; km/h = kilometers per hour. *p<0.05, **p<0.01.

DISCUSSION

It is known that pain tolerance threshold differs in luteal and follicular phases, and that women bear less pressure pain at different points of the body during follicular phase²⁰. This phenomenon was identified in this study. Women from our sample bore on average, 31% less pressure at the 16 points assessed by algometry. Moreover, although several studies have indicated losses in functional capacity due to physical pain in follicular phase, the present study provides unprecedented data of cardiorespiratory and metabolic parameters obtained by ergospirometry.

Although the exact mechanisms are still unclear, female gonadal hormones interact with nociceptive processes at multiple levels of the peripheral and central nervous system, and variations in hormonal levels are associated with variations in pain experi-

ence⁶. Some hemodynamic determinants may also vary across the menstrual cycle, but they seem to be more influenced by epinephrine reactivity to stress than by sex hormones themselves²¹. There are indications of a strong inverse correlation between level of pain (measured by VAS) and performance in a physical exercise on treadmill ($r=0.69$, $p=0.01$)⁷. Chantler, Mitchell and Fuller⁷ et al.,⁷ showed that women with dysmenorrhea pain exhibited significantly less time of test (Bruce protocol), decreased muscle strength (1 repetition maximal in leg press exercise at 45°) and more time to perform an exercise (bending down and getting up carrying a load) in comparison to controls (in use of anti-inflammatory drug). Oral administration of diclofenac potassium (50mg), a nonsteroidal anti-inflammatory drug (inhibitor of prostaglandins) suppressed these declines. Similar results were found in this study. Although there was no significant reduction in test duration, follicular phase resulted in losses ranging from 3.7 to 17.6% in the peak HR (3.9%), peak VO₂ (12.8%), and VO₂ at RCP (17.6%), without significant changes in AT, ventilatory efficiency (VE/VO₂ and VE/VCO₂) and rate of gas exchange (RQ). Together, these results indicate that the prejudice in cardiorespiratory fitness in follicular phase was related to oxygen consumption and ventilatory efficiency or changes in the use of energy substrates (RQ). Additionally, at rest, there was a significant increase in systolic and diastolic BP (7.4 and 11.8%, respectively), indicating a greater hemodynamic stress in follicular phase.

Pain is a very complex phenomenon and depends on cognition, emotion, environment and biological status of nerve structures²². Although a limitation of this study might be the sample size, we sought to standardize the sample so it was as homogeneous as possible, as women from our study had little variation in age, were students of health courses (with similar cognition), inserted in the same university context and had no other possible bias such as contraceptive use and previous uterine diseases. However, dysmenorrhea was assessed by self-report, which does not allow full discrimination between primary or secondary dysmenorrhea.

If the menstrual cycle is relevant to the determination of painful symptoms, it must be considered as a factor influenced by women's pain experience²⁰. In the present study, we sought to evaluate this experience through dolorimetry. This type of evaluation, using a digital algometer, is considered a gold standard for the measurement of pressure pain sensitivity²³. With respect to the sites assessed by algometry in this study, it was found that different areas of the pelvic region and muscles of the upper limbs and trunk were also negatively influenced in the follicular phase, revealing that hormonal changes affect pain tolerance in general. In a way, our results counteract a recent review pointing out that currently, most studies show that menstrual cycle has no effect on pain perception in healthy women⁶. However, unravelling the present findings, the authors of the review study⁶ acknowledge that hormonal interaction and pain perception are complex and not fully understood. Adding to the findings of the influence of menstrual cycle on pain, cardiorespiratory capacity also presented worse results in follicular phase. Although a previous study has not found differences in other physical capacities such as flexibility¹, muscle strength and endurance⁸, anaerobic performance, and walking speed⁹, this study revealed that, with respect to cardiorespiratory

fitness, evaluated by a progressive maximal cardiopulmonary exercise test, several parameters are negatively affected by pain.

Reduction in exercise performance associated to increased pain sensitivity may have important repercussions in daily living activities, social life and quality of life of women, as previously observed by authors who studied pain in follicular phase^{24,25}. Despite this finding, women should not avoid exercising in follicular phase, as exercise contributes to the reduction of dysmenorrhea symptoms⁴. Health professionals must provide orientations to women with dysmenorrhea about these physiological transitory changes that accompany menstrual cycles, as well as when and how to use pharmacological and non-pharmacological methods of pain management, in order to minimize the negative impacts in their quality of life.

CONCLUSION

Healthy women with dysmenorrhea show higher pain perception in follicular phase, which results in increased pain sensitivity and prejudice in hemodynamic aspects at rest and during exercise, as well as in cardiorespiratory fitness, without significant alterations in metabolism.

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