ARE THERE ANY DIFFERENCES IN PAIN THRESHOLDS DURING THE MENSTRUAL CYCLE?

POSTOJE LI RAZLIKE U PRAGU BOLA U RAZLIČITIM FAZAMA MENSTRUALNOG CIKLUSA?

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Original study
UDK 618.75:613.99
https://doi.org/10.2298/MPNS2408228S

Abstract

Introduction. Pain perception in women may vary due to hormonal fluctuations across the phases of the menstrual cycle. Emotional status also tends to fluctuate significantly during these phases. This study aimed to investigate differences in pressure pain thresholds between the follicular and luteal phases of the menstrual cycle. An additional objective was to evaluate variations in emotional status. **Material and Methods.** The phases of the menstrual cycle were determined using an online ovulation calculator. Participants in the ovulation phase (n=5) were excluded from further analysis. A total of 95 participants (mean age 27.7±7.8 years) were included in the study. Pressure pain threshold testing was conducted on the extensor carpi radialis longus muscle and the paraspinal musculature of the lumbar region using an algometer equipped with a 1 cm^2 rubber tip. The Depression, Anxiety, Stress Scale was employed to evaluate variations in emotional status. **Results.** No significant differences were observed in pressure pain thresholds in the forearm region (follicular phase (33.55 ± 12.15 N/cm^2) vs. luteal phase (33.55 ± 13.65 N/cm^2), t=0.509; p=0.979) or the lower back region (follicular phase (56.85 ± 19.95 N/cm^2) vs. luteal phase (58.93 ± 21.20 N/cm^2), t=0.982; p=0.619) between the follicular and luteal phases of the menstrual cycle. Similarly, no significant differences were identified in levels of depression (χ^2 = 1016.000; p = 0.392), anxiety (χ^2 = 972.500; p=0.243), or stress levels (t = -1.038; p=0.302) during the menstrual cycle. **Conclusion.** The findings indicate no significant variations in pressure pain thresholds or emotional status across different phases of the menstrual cycle.

Key words: Pain Perception; Pain Threshold; Menstrual Cycle; Emotional Regulation

Sažetak

Uvod. Percepcija bola kod žena može varirati usled hormonskih promena tokom različitih faza menstrualnog ciklusa. Takođe, tokom menstrualnog ciklusa može doći i do značajnih promena emocionalnog statusa. Cilj studije bio je da se utvrdi razlika u pragu bola na pritisak kod žena tokom folikularne i lutealne faze menstrualnog ciklusa. Dodatni cilj bio je da se procene razlike u emocionalnom statusu tokom menstrualnog ciklusa. **Materijal i metode.** Faza menstrualnog ciklusa utvrđena je pomoću onlajn ovulacionog kalkulatora. S obzirom da je samo pet ispitanica bilo u fazi ovulacije, one nisu uključene u dalju analizu. U istraživanje je uključeno 95 ispitanica (prosečne starosti 27,7 ± 7,8 godina). Testiranje praga bola pritiskom vršeno je na *m. extensor carpi radialis longus* i na paraspinalnoj muskulaturi lumbalnog dela kičmenog stuba koristeći algometar sa gumenim vrhom površine 1 cm^2. Za procenu emocionalnog statusa korišćena je Skala depresije, anksioznosti i stresa. **Rezultati.** Nisu zabeležene značajne razlike u pragu bola pritiskom na podlaktici (folikularna faza (33,55 N/cm^2 ± 12,15 N/cm^2) vs. lutealna faza (33,55 N/cm^2 ± 13,65 N/cm^2), t = 0,509; p = 0,979) i u lumbalnoj regiji (folikularna faza (56,85 N/cm^2 ± 19,95 N/cm^2) vs. lutealna faza (58,93 N/cm^2 ± 21,20 N/cm^2), t = 0,982; p = 0,619) među ispitanicama u folikularnoj i lutealnoj fazi menstrualnog ciklusa. Nisu pronađene značajne razlike u depresivnosti (χ^2 = 1016.000; p = 0.392), anksioznosti (χ^2 = 972.500; p = 0,243) i stresu (t = -1.038;p = 0.302) tokom menstrualnog ciklusa. **Zaključak.** Ne postoje značajne razlike u pragu bola na pritisak i emocionalnom statusu žena u različitim fazama menstrualnog ciklusa.

Ključne reči: percepcija bola; prag bola; menstrualni ciklus; emocionalna regulacija

Introduction

Pain is a complex physiological response of the sensory nervous system to actual or potential harmful stimuli [1]. The process of pain perception can be divided into four phases: transduction, transmission, modulation, and perception [2]. During transduction, nociceptors convert noxious stimuli into action potentials. In the transmission phase, nerve impulses travel along myelinated A-delta fibers and unmyelinated C fibers from nociceptors to the posterior horn of the spinal cord. These impulses are then relayed through ascending pathways to higher centers in the central nervous system. Modulation occurs when nociceptive signals are processed and modified in the dorsal horn of the spinal cord. Finally, in the perception phase, pain signals reach the cerebral cortex, resulting in the conscious experience of pain [3].

The menstrual cycle (MC) is a physiological process in women, commencing with menarche (the onset of menstruation) at puberty and continuing until menopause. A typical MC spans 28 to 30 days and

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Abbreviations

MC – menstrual cycle
FP – follicular phase
LP – luteal phase
QST – quantitative sensory testing
PPT – pressure pain threshold
DASS 21 – Depression Anxiety Stress Scale

is characterized by significant hormonal fluctuations [4]. The cycle is divided into three phases: the follicular phase (FP), ovulation, and the luteal phase (LP). The FP begins on the first day of menstruation and lasts approximately 14 days, during which ovarian follicles develop and produce estrogen. Ovulation occurs around day 14, when a mature egg is released and travels through the fallopian tube, ready for fertilization. The LP follows ovulation and lasts about 14 days, during which the ruptured follicle forms the corpus luteum, producing progesterone. In the absence of pregnancy, hormone levels decline, triggering menstruation [5]. Hormonal fluctuations throughout the MC have been linked to changes in emotional status, as suggested by some studies [6].

Pain is both sensory and emotional experience, and its perception varies significantly among individuals [7]. Numerous factors influence pain perception, including spontaneous neural activity, expectations, sleep patterns, emotional stress, and stress levels [8–11]. Gonadal hormones play a pivotal role in this variability, contributing to differences not only between men and women [12], but also among women themselves [13].

Quantitative sensory testing (QST) is a diagnostic method to evaluate somatosensory function through various tests [10]. One QST method is pressure pain threshold (PPT) testing, which measures the minimum force required to elicit pain [14]. This semi-objective and efficient technique is a valuable and reliable tool for assessing pain thresholds [15].

Although previous studies have suggested that hormonal fluctuations during the MC may influence pain perception in women, findings remain inconsistent [16]. Therefore, this study aimed to evaluate differences in PPT between the FP and LP of the MC. Additionally, the study sought to assess variations in emotional status during these phases.

Material and Methods

This prospective case series study received approval from the Ethics Committee of the Faculty of Medicine at the University of Novi Sad (no. 01-39/7). Informed consent was obtained from all participants prior to their inclusion in the research. The study included women aged 18 years and older with no current pain. Exclusion criteria were: current use of analgesics, benzodiazepines, or antidepressants, presence of acute or chronic pain (headaches, injuries, etc.), severe cardiac, metabolic, or kidney diseases, neurological disorders, serious psychiatric conditions (schizophrenia, bipolar disorder, etc.), menopause, irregular menstrual cycles. Demographic and anthropometric data were collected including age, height, weight and educational level (years of education). Data on menstrual cycle duration and the number of days since the last menstruation were also gathered. Menstrual cycle phases we calculated using a tool provided by the U.S. Department of Health & Human Services [17].

Participants were instructed to abstain from sedatives, analgesics, alcohol, or intense physical activity 24 hours before testing. They were also advised to avoid consuming caffeine products within four hours of the test and ensure adequate sleep the night prior.

Testing followed the standard protocol routinely conducted in our laboratory [18–20]. Pressure pain threshold (PPT) was measured using a digital algometer (Wagner Instruments, FDX-50) with a 1 cm diameter rubber tip. After familiarizing participants with the procedure and equipment, testing commenced. PPT measurements were performed on the extensor carpi radialis longus muscle (5 cm distal to the lateral epicondyle of the humerus), and on the paraspinal musculature of the lumbar region (2-3 cm lateral to the L3 spinous process). The algometer pressure was gradually increased at a rate of 5 N/s, and participants were instructed to say "stop" when the sensation transitioned from pressure to pain, burning, stinging, or stabbing. The pressure value in N/cm^2 was recorded. Three measurements were taken at each site with a 10-second interval between them. The final result was the average of the three measurements. Both the left and right sides were tested alternately.

Participants completed the Depression, Anxiety, and Stress Scale (DASS-21), a tool for assessing levels of depression, anxiety, and stress. The DASS-21 contains 21 questions divided into three subscales, each comprising seven items. Participants rate their experiences over the previous week using a 4-point Likert scale. Higher scores indicated greater levels of depression, anxiety, and stress [21].

A priori analysis using G*Power 3.1 indicated a minimum required sample size of 82 participants to detect an effect size of 0.3, with $\alpha=0.05$ and a power of 0.8 [22, 23]. Data were analyzed using SPSS 23 software. Descriptive and inferential statistical methods were employed. Depending on the normality of the data distribution, the Student's t-test, the Mann-Whitney test, and χ^2 test were used for group comparisons. Statistical significance was set at $p \leq 0.05$.

Table 1. Demographic and anthropometric details of participants in relation to the menstrual cycle phase

	MC phase	Mean	Standard deviation	t/χ^2	p
Age (years)	FP	28.2	8.3	t=0.653	0.515
	LP	27.2	7.3		
Height (cm)	FP	168.4	5.5	χ^2=912.000	0.108
	LP	170.6	7.9		
Weight (kg)	FP	62.5	8.6	χ^2=1060.000	0.617
	LP	62.3	11.0		
Years of education	FP	16.03	2.495	t=0.678	0.501
	LP	15.65	1.495		

MC – menstrual cycle; FP –follicular phase; LP – luteal phase

Table 2. Pain threshold variations between participants in different phases of the menstrual cycle

	MC phase	Mean	Standard deviation	t	p
PPT Forearm (N/cm^2)	FP	33.55	12.15	t=0.509	0.979
	LP	33.55	13.65		
PPT Low back region (N/cm^2)	FP	56.85	19.95	t=0.982	0.619
	LP	58.93	21.20		

MC – menstrual cycle; FP –follicular phase; LP – luteal phase; PPT – pressure pain threshold

Table 3. Variations in depression, anxiety, and stress scores between participants in different phases of the menstrual cycle

	MC phase	Mean	Standard deviation	t/χ^2	p
DASS-21 Depression	FP	2.35	2.825	χ^2=1016.000	0.392
	LP	2.22	4.049		
DASS-21 Anxiety	FP	3.33	3.071	χ^2=972.500	0.243
	LP	2.85	3.353		
DASS-21 Stress	FP	7.08	5.408	t=-1.038	0.302
	LP	8.33	6.268		

MC – menstrual cycle; FP –follicular phase; LP – luteal phase; PPT – pressure pain threshold; DASS-21 – Depression Anxiety Stress Scale

Results

The study included 100 women. However, due to the small number of participants in the ovulation phase (n = 5), these individuals were excluded from further analysis. The final sample consisted of 95 participants (mean age 27.7 ± 7.8 years), with the majority being in the follicular phase (n = 49, 51.6%). The average menstrual cycle duration in the studied group was 28.99 ± 2.39 days. There were no significant differences between the follicular and luteal phase groups in terms of age (t=0.653; p=0.515), height (χ^2=912.000; p=0.108), weight (χ^2=1060.000; p=0.617), and years of education (t=0.678; p=0.501). Detailed demographic and anthropometric characteristics of the participants are presented in **Table 1.**

No significant differences were observed in PPT measurements for the forearm region (t=0.509; p=0.979) or the lower back region (t=0.982; p=0.619) between participants in the FP and LP of the MC. These results are summarized in **Table 2**.

Analysis of emotional status revealed no significant differences in levels of depression (χ^2=1016.000; p=0.392), anxiety (χ^2=972.500; p=0.243), or stress (t = -1.038; p=0.302) between the MC phases. Additional details are provided in **Table 3.**

Discussion

Pain is highly subjective and individual experience, influenced by a variety of physical, biological, and psychosocial factors [24–26]. Given the hormonal fluctuations during the menstrual cycle and their potential impact on pain perception [27], this study focused on healthy women without pain to investigate whether these changes affect pain thresholds.

The MC is regulated by hormones from the hypothalamus, pituitary gland, and ovaries [5]. Regularity and duration of the cycle serve as indicators of endocrine function and reproductive health [28]. Due to the small number of participants in the ovulation phase, this study compared only the FP and LP. The average MC length in our sample was 28.99 ± 2.39 days, aligning within the typical range of 25-30 days [29].

Hormonal fluctuations have been implicated in modulating women's pain thresholds, first reported by

Herren [30]. Since then, numerous studies have investigated the relationship between hormonal fluctuations and pain perception, with several suggesting that estrogen and progesterone lay significant roles [31, 32]. Estrogen, in particular, is recognized as a key pain modulator [33]. Smith et al. demonstrated a clear correlation between estradiol levels and pain thresholds, noting that high estrogen levels increase the number of opioid receptors, thereby enhancing the body's response to endorphins [34]. Progesterone, another critical sex hormone, acts synergistically with estrogen and exhibits both nociceptive and antinociceptive effects, depending on the MC phase [32]. Research on healthy women indicates heightened pain sensitivity during periods of low estrogen levels [35]. However, the prevailing consensus is that pain sensitivity is influenced not only by low estrogen levels but also by the dynamic fluctuations in these hormone levels, which can reduce pain thresholds [36, 37].

In contrasts to these findings, our results revealed no significant differences in PPT between the FP and LP. These results deviate from earlier studies that reported phase-dependent variations in pain perception. For example, Wiesenfeld-Hallin [38] and Riley et al. [39] observed higher pain thresholds during the FP and lower thresholds in the late LP. Stening [35] and Young-Hee et al. [40] also reported lower thresholds in the LP. Conversely, Martin et al. [41] reported greater pain sensitivity in the FP. These discrepancies may stem from methodological variations, including differences in pain stimuli, testing locations, and definitions of menstrual phases. Iacovides et al. [42] concluded in their review that current research does not provide conclusive evidence regarding the relationship between MC phases on pain perception.

Our study also assessed emotional status, finding no significant differences in depression, anxiety, or stress levels between the FP and LP. This is somewhat unexpected, as premenstrual syndrome (PMS), which is associated with the LP, affects up to 75% of reproductive-age women [6]. PMS includes both physical symptoms like fatigue, appetite changes, and low energy, as well as emotional symptoms such as irritability, depression, anxiety and impulsivity [43]. Hoyeret al. reported more pronounced symptoms of depression, anxiety, and stress during the LP, particularly in the late phase, which contrasts with our findings [44]. Recent literature supports the notion that emotional states are often exacerbated during the premenstrual and menstrual phases, with fluctuations in hormone levels playing a significant role [45]. Considering that previous studies suggest that depression, anxiety, and stress can lower pain thresholds and increase pain sensitivity [46–48], the question remains whether these psychological factors might have influenced the observed results in PPT during the FP and LP of the MC.

This study had several limitations. First, the small sample size for the ovulation phase prevented its inclusion in further analysis, even though this phase may exhibit the most pronounced decrease in pain threshold due to hormonal fluctuations [36]. Additionally, menstrual phases were determined using an online ovulation calculator, a simple and cost-effective method, but less accurate than more advanced techniques, such as blood hormone measurements or urine test strips [49, 50]. These methodological limitations may have influenced our findings and should be considered when interpreting the results.

Conclusion

Our study found no significant differences in pressure pain threshold or levels of depression, anxiety, and stress between the follicular phase and luteal phase of the menstrual cycle. These findings underscore the need for further research to elucidate the impact of menstrual cycle phases on pain thresholds.

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Rad je primljen 3. XII 2024.
Recenziran 16. XII 2024.
Prihvaćen za štampu 16. XII 2024.
BIBLID.0025-8105:(2024):LXXVII:7-8:228-233.

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