Medical Journal of Bakırköy

Med J Bakirkoy 2025;21(4):430-435
DOI: 10.4274/BMJ.galenos.2025.2025.1-22

Research

Does the Menstrual Cycle Affect Skin Puncture Pain During Spinal Anesthesia? Prospective, Observational Study

Menstural Siklus Spinal Anestezi Sırasında Deri Delinme Ağrısını Etkiler mi? Prospektif, Gözlemsel Çalışma

Mahmut Sami Tutar[1], Rabia Korkmaz[1], Şule Yaşayacak[1], Mustafa Atcı[2], Muhammed Halit Satıcı[1], Bülent Hanedan[1], Munise Yıldız[1], Betül Kozanhan[1]

[1]Konya City Hospital, Clinic of Anesthesiology and Reanimation, Konya, Türkiye

[2]Kozan State Hospital, Clinic of Anesthesiology and Reanimation, Adana, Türkiye

ABSTRACT

Objective: Skin puncture pain during spinal anesthesia is a significant concern for many patients and may lead to reluctance to choose this anesthetic method, affecting patient satisfaction and acceptance of the procedure. This study aimed to evaluate the effect of menstrual cycle phase on needle-insertion pain during spinal anesthesia.

Methods: This study included 80 female patients, aged 18-45 years, who underwent spinal anesthesia using a 25G Quincke-tipped needle at the L3-L4 or L4-L5 vertebral levels in the sitting position. Patients were divided into two groups: follicular phase and luteal phase. Upon completion of the procedure, pain during needle insertion was assessed using the Numerical Rating Scale (NRS).

Results: No statistically significant differences were observed between menstrual cycle phases and NRS scores during needle insertion (p=0.804). Additionally, no significant correlation was found between NRS scores and body mass index (r=-0.109, p=0.335). However, a weak but statistically significant negative correlation was identified between NRS scores and age (r=-0.246, p=0.028).

Conclusion: The findings indicate that the phase of the menstrual cycle does not influence needle insertion pain during spinal anesthesia and emphasize that other factors, such as age, might have a minor impact on pain perception.

Keywords: Oestrogen, menstrual cycle, spinal anesthesia, skin puncture pain

ÖZ

Amaç: Spinal anestezi sırasında deri delme ağrısı birçok hasta için önemli bir endişe kaynağıdır ve bu anestezi yöntemini seçmede isteksizliğe yol açarak hasta memnuniyetini ve prosedür kabulünü etkileyebilir. Bu çalışma, adet siklusunun spinal anestezi sırasında iğne yerleştirme ağrısı üzerindeki etkisini değerlendirmeyi amaçladı.

Gereç ve Yöntem: Bu çalışmaya, oturma pozisyonunda L3-L4 veya L4-L5 vertebra seviyelerinde 25G Quinke uçlu iğne kullanılarak spinal anestezi uygulanan 18-45 yaş arası 80 kadın hastalar dahil edildi. Hastalar foliküler ve luteal faz olmak üzere iki gruba ayrıldı. İşlem tamamlandıktan sonra, iğne yerleştirme sırasındaki ağrı Sayısal Derecelendirme Ölçeği (SDÖ) kullanılarak değerlendirildi.

Bulgular: İğne yerleştirme sırasında adet siklusu ve SDÖ skorları arasında istatistiksel olarak anlamlı bir fark gözlenmedi (p=0,804). Ek olarak, SDÖ skorları ve vücut kitle indeksi arasında anlamlı bir korelasyon bulunmadı (r=-0,109, p=0,335). Ancak, SDÖ puanları ile yaş arasında zayıf ancak istatistiksel olarak anlamlı bir negatif korelasyon tespit edildi (r=-0,246, p=0,028).

Sonuç: Bulgular, adet siklusunun spinal anestezi sırasında iğne batırma ağrısını etkilemediğini, yaş gibi diğer faktörlerin ağrı algısı üzerinde küçük bir etkiye sahip olabileceğini vurgulamaktadır.

Anahtar Kelimeler: Östrojen, adet siklusu, spinal anestezi, deri delinme ağrısı

Address for Correspondence: Muhammed Halit Satıcı, MD, Konya City Hospital, Clinic of Anesthesiology and Reanimation, Konya, Türkiye
E-mail: halit_satici@hotmail.com **ORCID ID:** orcid.org/0009-0005-0652-3624

Cite as: Tutar MS, Korkmaz R, Yaşayacak Ş, Atcı M, Satıcı MH, Hanedan B, et al. Does the menstrual cycle affect skin puncture pain during spinal anesthesia? Prospective, observational study. Med J Bakirkoy. 2025;21(4):430-435

Received: 27.01.2025
Accepted: 13.05.2025
Publication Date: 18.12.2025

INTRODUCTION

Pain perception varies significantly among individuals and is influenced by biological, psychological, and social factors. Among these, sex-based differences in pain sensitivity have been extensively studied. Women consistently demonstrate greater pain sensitivity than men, attributed to variations in the endogenous opioid system, hormonal fluctuations, and psychosocial factors (1). Hormonal cycles unique to women, particularly the perimenstrual phase, are associated with heightened pain sensitivity, systemic inflammatory responses, and conditions such as vocal cord edema and peripheral edema (2). Additionally, women are more likely to experience postoperative complications, including nausea, vomiting, sleep disturbances, reduced intravenous anesthetic requirements, and delayed gastric emptying, particularly during the luteal phase, when cyclical fluctuations in hormones such as progesterone occur (2-4).

Despite evidence linking menstrual cycles to pain and physiological changes, limited research has explored their impact on procedural pain. Spinal anesthesia, a cornerstone in neuraxial blocks for lower body surgeries, is effective and widely used (5). However, the potential influence of the menstrual cycle on pain during spinal needle insertion remains underexplored. This study aims to investigate the relationship between the menstrual cycle and pain during spinal needle insertion in women of reproductive age undergoing elective surgery, with the aim of providing insights to improve patient comfort and guide clinical practice.

METHODS

Ethics Approval and Registration

Ethical approval for the study was obtained from the Ethics Committee of University of Health Sciences Türkiye, Hamidiye Scientific Research Ethics Committee (approval no: 16/2, date: 17.06.2022). It was registered on ClinicalTrials.gov (identifier: NCT05481255). The study was conducted using the principles of the Declaration of Helsinki and adhered to CONSORT guidelines (6,7). Written informed consent was obtained from all participants.

Patient Population and Inclusion/Exclusion Criteria

The inclusion criteria for the study consist of female patients aged 18-45 years who are undergoing a single-attempt spinal anesthesia with a 25G Quincke-tipped needle at the L3-L4 or L4-L5 vertebral levels in the sitting position, who are classified as American Society of Anesthesiologists physical status I or II, and who have had regular menstrual cycles for at least the past six months. The exclusion criteria include pregnancy, use of oral contraceptives, an anxiety subscale score on the Hospital Anxiety and Depression Scale (HADS) of 10 or higher, or a depression subscale score of 7 or higher (8,9).

Study Protocol

The patients' anxiety and depression levels were assessed using the 14-item HADS, which was administered by one of the researchers (M.Y.) on the morning of surgery prior to spinal anesthesia. Each participant was asked about the first day of their last menstrual period and the duration of their menstrual cycle to calculate the specific day within that cycle. Based on this information, patients were categorized into two groups: the follicular-phase group (cycle days 8-10) and the luteal-phase group (cycle days 18-20). Spinal anesthesia was administered by an experienced anesthesiologist (B.H.) who was not involved in either the data collection or group allocation processes. After the procedure, a second researcher (Ş.Y.), who was blinded to the patient's menstrual cycle phase, asked the patient to rate the pain during the skin puncture using the Numerical Rating Scale (NRS), where 0 indicated no pain and 10 represented the worst imaginable pain. Finally, a third researcher (B.K.) independently verified the menstrual cycle phase by re-evaluating the date of the last menstrual period and cycle duration provided by the patient.

Statistical Analysis

Sample size analysis was performed based on the patient's NRS score for skin-puncture pain during the spinal procedure. A 30% score difference between the groups was considered significant. Using a Cohen's d effect size of 0.670 in the independent-groups t-test model based on pilot data, it was calculated that 36 patients in each group (a total of 72 patients) should participate in the study to achieve 80% power with a maximum 5% type I error. Accounting for a 10% dropout rate, the required sample size was 80 participants.

The data obtained in the study were analyzed using the International Business Machines statistical package for the social sciences (IBM SPSS Inc., Chicago, IL, USA), version 26.0. The normality of the data distribution was evaluated using the Shapiro-Wilk test. Continuous variables were presented as mean and standard deviation or median (25^{th}-75^{th} percentiles), while categorical variables were expressed as numbers and percentages. For the analysis of continuous variables, the Independent samples t-test was employed when parametric test assumptions were met; otherwise, the Mann-Whitney U test was utilised. The relationship between NRS scores and patient characteristics was analysed using Spearman's rho. Statistical significance was accepted at $p<0.05$.

RESULTS

In this study, 105 cases were screened for eligibility based on the inclusion criteria. Fifteen patients were excluded for lack of consent to participate, and an additional ten were excluded for exceeding the cut-off on the HADS. Specifically, these patients had elevated HADS scores prior to spinal anesthesia. Consequently, the remaining 80 patients were included in the final analysis, with 40 allocated to the follicular-phase group and 40 to the luteal-phase group. A flowchart outlining the study process is presented in Figure 1.

An evaluation of patient characteristics based on menstrual cycle phase revealed no statistically significant differences in age, height, weight, or body mass index (BMI) between the follicular-phase and luteal-phase groups (p>0.05). Similarly, there were no significant differences between groups in preoperative HADS anxiety and depression scores (p=0.464 and p=0.661, respectively). The NRS scores for needle insertion pain were also comparable between groups (p=0.804; Table 1).

Further analysis of the relationship between NRS scores and patient characteristics revealed a weak but statistically significant negative correlation between NRS scores and age (r=-0.246, p=0.028). However, no significant correlations were observed between NRS scores and height, HADS anxiety scores, or HADS depression scores (r=0.04, p=0.725; r=0.085, p=0.455; and r=0.135, p=0.233, respectively). Similarly, weight and BMI showed weak negative correlations with NRS scores that were not statistically significant (weight: r=-0.082, p=0.469; BMI: r=-0.109, p=0.335) (Table 2).

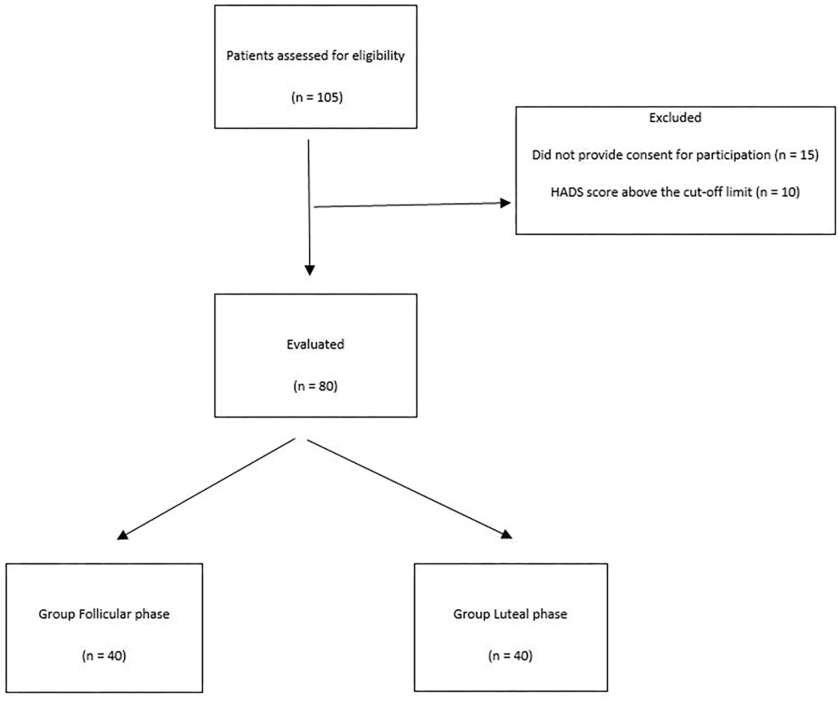

Figure 1. The flowchart of the study
HADS: Hospital Anxiety and Depression Scale

Table 1. Evaluation of patient characteristics according to menstrual cycle

Characteristic	Folicular phase (n=40)	Luteal phase (n=40)	p-value
Age	31.38±6.63	33.53±6	0.133
Height (cm)	162.62±5.57	163.80±6.59	0.392
Weight (kg)	69.85±12.62	69.25±11.65	0.826
BMI (kgm^2)	26.39±4.40	25.92±4.69	0.649
HADS anxiety score	3 (2-5)	3 (2-5)	0.464
HADS depression score	3 (2-5)	3 (2-4.5)	0.661
NRS score	2 (1-3.5)	2 (1-3)	0.804

Statistical test applied: independent samples t-test and the Mann-Whitney U test. Values are presented as mean±standard deviation or median (25-75 percentiles).
BMI: Body mass index, HADS: Hospital Anxiety and Depression Scale and NRS: Numerical Rating Scale

Table 2. Relationship between NRS score and patient characteristics

NRS score		
Characteristic	**r-value**	**p-value**
Age	-0.246	0.028
Height (cm)	0.04	0.725
Weight (kg)	-0.082	0.469
BMI (kgm^2)	-0.109	0.335
HADS anxiety score	0.085	0.455
HADS depression score	0.135	0.233

Statistical test applied: Spearman rho correlation test.
BMI: Body mass index, HADS: Hospital Anxiety and Depression Scale, NRS: Numerical Rating Scale and r: correlation coefficient

DISCUSSION

This study demonstrated that the menstrual cycle phase did not significantly influence pain intensity measured by the NRS. This finding suggests that hormonal fluctuations associated with the menstrual cycle may not play a clinically relevant role in modulating acute procedural pain during spinal anesthesia. Additionally, a weak but statistically significant negative correlation was observed between NRS scores and age, indicating that older patients tend to report slightly lower pain levels.

Spinal anesthesia is a widely used neuraxial technique in which local anesthetic is injected into the cerebrospinal fluid within the subarachnoid space of the lumbar spine. While it is generally well tolerated, pain during spinal needle insertion remains a concern for some patients, especially those with increased pain sensitivity. Spinal needle insertion activates nociceptive pathways by stimulating peripheral nerve endings in the skin and underlying tissues. Pain perception during such procedures is primarily mediated by A-delta and C fibers, which transmit noxious stimuli to the dorsal horn of the spinal cord (10,11). These impulses are then relayed through second-order neurons via the spinothalamic tract to higher brain regions, including the thalamus and somatosensory cortex, where pain is consciously perceived. The periaqueductal gray matter and descending inhibitory pathways also play a key role in modulating the pain response (10,11).

Hormonal fluctuations during the menstrual cycle, particularly changes in estrogen and progesterone levels, may influence the sensitivity of these pathways. Estrogen is known to modulate both peripheral and central nociceptive processing by interacting with opioid receptors, N-methyl-D-aspartate receptors, and serotonin pathways (12). Some studies suggest that high or fluctuating estrogen levels may enhance pain perception, while others indicate a protective analgesic effect depending on the context (12-14). Understanding these complex hormonal influences is essential when evaluating procedural pain in women during different phases of the menstrual cycle.

Pain associated with spinal needle puncture is a critical concern. These concerns highlight the importance of addressing procedural pain and improving patient education to alleviate fears related to spinal anesthesia (15).

Skin puncture can cause both physical and psychological distress, with multiple factors influencing pain perception. Physiologically, puncture activates nociceptive pathways, leading to the sensation of pain. Psychological factors such as fear of needles, anticipation of pain, and procedural unpredictability play significant roles. Fear and anxiety can heighten pain perception by activating the body's stress response, which amplifies the central nervous system's sensitivity. Moreover, pain experienced during a procedure can reinforce anxiety, creating a cycle of heightened distress in future interventions (16). It is well-documented that women generally exhibit lower pain thresholds compared to men (17,18). Women also report higher rates of discomfort and demonstrate reduced pain tolerance across various settings (17). These differences arise from biological and neurophysiological variability in nociceptive processing between the sexes. Females may display heightened sensitivity to experimentally induced pain and increased temporal summation of mechanically evoked pain, indicating a more pronounced response to repeated or sustained nociceptive stimuli (19).

One explanation for these differences lies in the influence of sex hormones, such as oestrogen and progesterone, which play a critical role in modulating pain perception. Oestrogen, in particular, interacts with opioid and serotonin receptors, impacting both the peripheral and central pain pathways. These hormonal fluctuations may contribute to variations in pain sensitivity at different points in the menstrual cycle, as well as to the increased prevalence of specific pain syndromes in women. For instance, research has identified a potential link between hormonal changes and the occurrence of particular types of headaches, such as migraines. Oestrogen's role in regulating vascular tone, inflammation, and nociception may explain its involvement in triggering or exacerbating headache disorders (20).

These findings highlight the importance of considering sex-based differences in pain perception and the role of hormonal influences when developing personalised pain management strategies for men and women. Numerous studies have investigated the relationship between the menstrual cycle and the prevalence or intensity of migraine

headaches, given the well-established influence of hormonal fluctuations on pain perception (21,22). However, findings from these studies have been inconsistent, reflecting the complexity of hormonal interactions with pain mechanisms (20).

Cao et al. (23) highlighted that oestrogen could enhance visceral pain sensitivity by modulating peripheral and central nociceptive pathways. This suggests that elevated oestrogen levels during certain phases of the menstrual cycle may increase pain perception in specific contexts. Conversely, Maleki et al. (24) proposed that decreased oestrogen levels, combined with elevated hypothalamic prostaglandin levels during the luteal phase, might trigger migraine episodes.

Tutar et al. (25) conducted a retrospective study of patients undergoing spinal anesthesia and found no significant.

Although hormonal fluctuations during the menstrual cycle have long been hypothesized to modulate nociceptive sensitivity, the findings of the present study did not reveal a significant association between the menstrual cycle and procedural pain during spinal anesthesia. This aligns with previous research suggesting that cyclical hormonal changes may not exert a clinically relevant effect on acute nociceptive responses, particularly in the context of localised, short-duration interventions such as needle penetration. The absence of a significant difference between the follicular and luteal phases indicates that factors other than hormonal status, such as individual pain thresholds, psychological state (e.g., anxiety), or procedural technique, may play a more substantial role in shaping pain perception during neuraxial anesthesia. Consequently, these results suggest that routine consideration of the menstrual cycle in anesthetic planning for women of reproductive age may not be necessary. However, the broader influence of sex hormones on pain remains a complex and multifactorial topic, and the present findings should not preclude individualized patient assessment. Instead, they highlight the importance of tailoring perioperative care to patient-specific characteristics rather than relying solely on biological cycles that may have limited predictive value in acute procedural settings.

Anxiety can influence pain perception through neurotransmitters such as gamma-aminobutyric acid, serotonin, noradrenaline, oxytocin, and endocannabinoids, which regulate anxiety and nociceptive pathways (26). Despite this connection, no significant correlation was identified between anxiety and needle penetration pain.

Age-related differences in pain perception remain inconsistent in the literature. While some studies suggest increased pain sensitivity in older adults due to changes in central processing, others propose a decline in pain sensitivity with age, possibly related to reduced nociceptive receptor density or slower nerve conduction (27,28). In this study, a weak but significant negative correlation between age and needle penetration pain was observed, indicating that older patients may experience slightly less pain. This finding aligns with research suggesting reduced nociceptive sensitivity in ageing populations and highlights the importance of considering demographic factors in procedural pain management.

Study Limitations

This study has several limitations. First, the oestrogen and progesterone levels of the patients were not measured using quantitative methods, which limits the ability to directly correlate hormonal fluctuations with pain perception. Second, as spinal anesthesia at the institution was predominantly performed using 25-gauge needles, this study exclusively included patients who underwent the procedure with this needle size.

Another limitation of this study is the lack of information regarding patients' prior experiences with spinal or epidural anesthesia. Since pain perception and behavioral responses can be shaped by previous exposure and learning, this may have influenced individuals' pain reporting.

CONCLUSION

In conclusion, this study demonstrated that the menstrual cycle phase did not significantly influence needle penetration pain during spinal anesthesia in women of reproductive age. While age exhibited a weak negative correlation with pain perception, the clinical significance of this finding requires further exploration. By advancing understanding of the factors affecting procedural pain, this research underscores the importance of personalized approaches to anesthesia care, ultimately aiming to improve patient satisfaction and outcomes.

ETHICS

Ethics Committee Approval: Ethical approval for the study was obtained from the Ethics Committee of University of Health Sciences Türkiye, Hamidiye Scientific Research Ethics Committee (approval no: 16/2, date: 17.06.2022).

Informed Consent: Patients provided both written and verbal consent.

FOOTNOTES

Authorship Contributions

Surgical and Medical Practices: M.S.T., M.H.S., Concept: M.S.T., B.K., Design: M.A., M.Y., Data Collection or Processing: R.K., Ş.Y., Analysis or Interpretation: M.S.T., B.H., Literature Search: M.S.T., M.A., Writing: M.S.T., B.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

REFERENCES

1. Bartley EJ, Fillingim RB. Sex differences in pain: a brief review of clinical and experimental findings. Br J Anaesth. 2013;111:52-8.
2. Kurdi MS, Ramaswamy AH. Does the phase of the menstrual cycle really matter to anaesthesia? Indian J Anaesth. 2018;62:330.
3. Tutar MS, Sekmenli N, Erol G, Karaarslan E, Yildiz M, Kozanhan B. Does the menstrual phase affect gastric emptying? Prospective, observational study. Eur Rev Med Pharmacol Sci. 2023;27:1989-95.
4. Clarke BL, Khosla S. Female reproductive system and bone. Arch Biochem Biophys. 2010;503:118-28.
5. Wulf HF. The centennial of spinal anesthesia. Anesthesiology. 1998;89:500-6.
6. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA. 2013;310:2191-4.
7. Moher D, Hopewell S, Schulz KF. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c869.
8. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983; 67:361-70.
9. Aydemir Ö, Guvenir T, Kuey L, Kultur S. Validity and reliability of Turkish version of hospital anxiety and depression scale. Turk Psikiyatri Derg. 1997;8:280-7.
10. Dowlati E. Spinal cord anatomy, pain, and spinal cord stimulation mechanisms. Semin Spine Surg. 2017;29:136-46.
11. Wahezi SE, Hanstein R, Spray DC. Understanding the pathways of pain. In: Sharan A, Tang SY, Vaccaro AR, editors. Basic Science of Spinal Diseases. New Delhi: Jaypee Brothers Medical Publishers; 2013. p. 95-118.
12. Aloisi AM. Gonadal hormones and sex differences in pain reactivity. Clin J Pain. 2003;19:168-74.
13. Craft RM. Modulation of pain by estrogens. Pain. 2007;132:S3-12.
14. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, and pain: a review of recent clinical and experimental findings. J Pain. 2009;10:447-85.
15. Gajraj NM, Sharma S, Souter AJ, Pole Y, Sidawi E. A survey of patients who refuse regional anesthesia. Anesth Analg. 1994;78:S126.
16. Kumar S, Gautam SKS, Gupta D, Agarwal A, Dhirraj S, Khuba S. The effect of Valsalva maneuver in attenuating skin puncture pain during spinal anesthesia: a randomized controlled trial. Korean J Anesthesiol. 2016;69:27-31.
17. Vallerand AH, Polomano RC. The relationship of gender to pain. Pain Manag Nurs. 2000;1(Suppl 1):8-15.
18. Wandner LD, Scipio CD, Hirsh AT, Torres CA, Robinson ME. The perception of pain in others: how gender, race, and age influence pain expectations. J Pain. 2012;13:220-7.
19. Sarlani E, Farooq N, Greenspan JD. Gender and laterality differences in thermosensation throughout the perceptible range. Pain. 2003;106:9-18.
20. Sun LH, Zhang WX, Xu Q, Wu H, Jiao CC, Chen XZ. Estrogen modulation of visceral pain. J Zhejiang Univ Sci B. 2019;20:628-36.
21. MacGregor EA, Igarashi H, Wilkinson M. Headaches and hormones: subjective versus objective assessment. Headache Q Curr Treat Res. 1997;8:126-36.
22. MacGregor EA, Frith A, Ellis J, Aspinall L, Hackshaw A. Prevention of menstrual attacks of migraine: a double-blind placebo-controlled crossover study. Neurology. 2006;67:2159-63.
23. Cao DY, Bai G, Ji Y, Traub RJ. Epigenetic upregulation of metabotropic glutamate receptor 2 in the spinal cord attenuates oestrogen-induced visceral hypersensitivity. Gut. 2015;64:1913-20.
24. Maleki N, Linnman C, Brawn J, Burstein R, Becerra L, Borsook D. Her versus his migraine: multiple sex differences in brain function and structure. Brain. 2012;135:2546-59.
25. Tutar MS, Korucu D, Ciftci C, Kozanhan B. The relationship between serum estrogen concentration and post-dural puncture headache: a retrospective study. Eur Rev Med Pharmacol Sci. 2023;27:2250-55.
26. Gross C, Hen R. The developmental origins of anxiety. Nat Rev Neurosci. 2004;5:545-52.
27. Rittger H, Rieber J, Breithardt OA, Dücker M, Schmidt M, Abbara S, et al. Influence of age on pain perception in acute myocardial ischemia: a possible cause for delayed treatment in elderly patients. Int J Cardiol. 2011;149:63-7.
28. Lautenbacher S, Kunz M, Strate P, Nielsen J, Arendt-Nielsen L. Age effects on pain thresholds, temporal summation and spatial summation of heat and pressure pain. Pain. 2005;115:410-8.