



Perimenstrual headache: migraine without aura or premenstrual syndrome symptom?

Perimenstrualna glavobolja: migrena bez aure ili simptom predmenstrualnog sindroma?

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Abstract

Background/Aim. Definition of menstrual migraine as a specific clinical entity or, maybe, migraine headache with menstrually related occurring, still remains unresolved question. The aim of this study was to investigate if perimenstrual headache in our patients fulfills diagnostic criteria for migraine without aura or represents a different type of headache which is the symptom of premenstrual syndrome (PMS). **Methods.** The study included 50 women with headache in perimenstrual period in at least two out of three menstrual cycles, during the last year or longer. Two questionnaires, a questionnaire for headache and a questionnaire for PMS, were used. **Results.** The majority of all the examined women, 29 of them, had migraine and PMS and 9 women had migraine without PMS. Headache in 38 (76.0%) patients fulfilled diagnostic criteria for menstrual migraine, (26 and 12 women had pure menstrual migraine and menstrually related migraine respectively). Intensity of PMS was not different in a groups of women with different types of headache ($p = 0.184$): a total number of PMS symptoms was 8.2 ± 4.6 in the group with pure menstrual migraine, 10.8 ± 3.9 in the group with menstrually related migraine and 10.8 ± 6.3 in the group with non-migraine headache. **Conclusion.** This study shows that headache, occurring in perimenstrual period, is not always migraine, but could fulfill criteria for tension-type headache, as well. Specific characteristics of perimenstrual headache, which could distinguish it as a symptom of PMS, were not found. Expected relation in time of headache onset and menarche was not confirmed.

Key words: migraine disorders; headache; diagnosis; questionnaires; premenstrual syndrome; quality of life; psychology, medical.

Apstrakt

Uvod/Cilj. Još uvek nije jasno da li menstrualna migrena predstavlja zaseban klinički entitet ili je reč o migrenskoj glavobolji koja se specifično javlja u menstrualnom periodu. Cilj ovog istraživanja bio je da se utvrdi da li perimenstrualna glavobolja ispitanih bolesnica ispunjava dijagnostičke kriterijume Međunarodne klasifikacije glavobolja (MKG) za migrenu bez aure ili predstavlja glavobolju drugih, nemigrenskih osobina koja se javlja kao simptom predmenstrualnog sindroma (PMS). **Metode.** Istraživanjem je bilo obuhvaćeno 50 žena sa glavoboljom u perimenstrualnom periodu u najmanje dva od tri menstrualna ciklusa tokom poslednjih godinu dana ili duže. Istraživanje je urađeno pomoću dva strukturisana upitnika: Upitnika za glavobolju i Upitnika za PMS. **Rezultati.** Najveći broj ispitivanih žena, njih 29, imalo je migrenu i PMS, dok je migrena bez PMS-a zabeležena kod devet ispitanica. U ispitivanoj grupi, glavobolja kod 38 žena (76,0%) ispunjavala je dijagnostičke kriterijume za menstrualnu migrenu, od čega je 26 žena imalo čistu menstrualnu migrenu, a 12 migrenu povezanu sa menstruacijom. Stepenn izraženosti PMS-a nije se razlikovao među grupama žena sa različitim tipovima glavobolje ($p = 0,184$): žene sa čistom menstrualnom migrenom imale su prosečno $8,2 \pm 4,6$, žene sa menstrualno povezanom migrenom $10,8 \pm 3,9$, a žene sa glavoboljom nemigrenskih osobina $10,8 \pm 6,3$ simptoma PMS-a. **Zaključak.** Ovim istraživanjem pokazano je da glavobolja koja se javlja u perimenstrualnom periodu nije obavezno migrena, već se javlja i kao glavobolja tenzionog tipa. Posebne osobine perimenstrualne glavobolje, na osnovu kojih bi ona mogla biti tumačena kao simptom PMS-a, nisu uočene. Ovim istraživanjem nije potvrđena očekivana vremenska povezanost menarhe i pojave prve glavobolje.

Ključne reči: migrena; glavobolja; dijagnoza; upitnici; premenstrualni sindrom; kvalitet života; psihologija, medicinska.

Introduction

Migraine is a type of headache with recurrent attacks of unilateral, pulsating pain of high intensity which aggravate with physical activity and is accompanied by photo- and/or phonophobia and nausea and/or vomiting. Menstruation is claimed to be one of the trigger factors for migraine attack in more than half of in-hospital examined patients with migraine and, according to population based studies, in more than a quarter of women with migraine¹. Headache gets worsen in 60% of women with migraine during the perimenstrual period, e.g. two days before and the first three days of menstrual bleeding, and some women, in smaller percent, report the headache attacks occurring exclusively in this period^{2,3}. Menstrual migraine exists as a pure menstrual and menstrually related migraine⁴. Patients with pure menstrual migraine report migraine attacks exclusively two days before or during the first three days of menstrual bleeding, and women with menstrually related migraine have additional pain attacks in other time of menstrual cycle, in at least two out of three menstrual cycles, for both diagnosis.

Pre-menstrual syndrome (PMS), according to the American College for Gynecology and Obstetrics, consists of physical and psychological symptoms and signs, occurring during at least five days before menstrual bleeding and completely resolving in four days after the bleeding onset, in at least three consecutive menstrual cycles⁵. More than 50% of women with PMS has headache as one of the symptoms⁶, but, exact clinical characterisation of type of this headache was not given.

There is not enough data which explain if menstrual migraine is specific type of headache, or simply migraine without aura, occurring in menstrual period. Also, there is none specific biomarker which can be used for differentiation menstrual and other types of migraine.

The aim of this study was to investigate if perimenstrual headache in our patients corresponds with diagnostic the International Classification of Headache Disorders (ICHD) criteria for migraine without aura or represents a different type of headache which is the symptom of PMS.

Methods

This study included 50 women with headache in perimenstrual period in at least two out of three menstrual cycles, during the last year or longer. All the patients were recruited in the Headache Center, Institute of Neurology, Belgrade, in the period from January 2006 to January 2008. Exclusion criteria for this study were pregnancy, ongoing hormonal or prophylactic therapy of migraine. Cases of symptomatic headache were excluded by neurological examination, laboratory blood testing, ophthalmological examination, electroencephalography (EEG), computed tomography (CT) and nuclear magnetic resonance (NMR) brain examinations. Two questionnaires, a questionnaire for headache and a questionnaire for PMS, were used.

Clinical characteristics of perimenstrual headache were estimated by, for this survey designed, the original Question-

naire for Headache (Attachment 1), and diagnosis of migraine without aura was given according to IHC diagnostic criteria. Frequency of headache attacks was recorded in perimenstrual period, but in other time of menstrual cycle as well and quantified as number of days with headache in one month period. Intensity of pain was estimated using the verbal analog scale (VAS, with 0 for notification of total absence of pain, and 10 for the pain with maximum of its intensity) (Attachment 2). According to data recorded using the Questionnaire for Headache, all patients were divided into three groups: women with pure menstrual migraine, with menstrually related migraine and with non-migraine headache. In these groups, we analysed the intensity of PMS and demographic features of patients.

Diagnosis of PMS was given using the Questionnaire for PMS, modification of the Moos's Menstrual Distress Questionnaire⁷. Using this questionnaire, we recorded physical and psychological symptoms and signs, occurring during at least five days before menstrual bleeding, persisting or vanishing during menstruation and completely resolving in four days after the bleeding onset, in at least three consecutive menstrual cycles. Intensity of PMS was quantified as a sum of points given for every symptom and sign. A maximum of points was 28. Diagnosis of severe PMS was given to patients with more than 20 points, of moderate PMS to those with 11 to 20 points, of mild PMS to those with 6 to 10 points, and a sum of less than 6 points indicated that a patient did not have PMS. According to the results of this questionnaire, all the examined women were divided into two groups: women with and without PMS. In these groups we analysed clinical characteristics of headache and demographic features of patients.

Statistical analyses of data was done in SPSS v.16.0.p.m programme, using Student's *t*-test, ANOVA and χ^2 test. Test value $p < 0.05$ was considered to be statistically significant.

Results

According to diagnosis of migraine without aura and PMS, four groups have been formed: women with migraine and PMS, with migraine and without PMS, and with non-migraine headache and PMS, and with non-migraine headache and without PMS. The majority of examined women, 29 of them, had migraine and PMS, and 9 patients had migraine without PMS. Non-migraine headache with PMS was present in 10 women, and non-migraine headache without PMS was recorded in only two cases. Demographic features of patients and the clinical characteristics of headache in these groups are given in Table 1.

Demographic features of patients and characteristics of headache were not significantly different in the groups of patients with perimenstrual headache (Table 1).

In 38 (76.0%) of all the examined women, headache fulfilled the IHC diagnostic criteria for menstrual migraine, with diagnosis of pure menstrual migraine in 26, and menstrually related migraine in 12 of them. Demographic features of patients and the clinical characteristics of headache in women with menstrual migraine are given in Table 2.

Table 1
Demographic features and clinical characteristics of headache in women with perimenstrual headache according to diagnosis of migraine and PMS

Parameters	Groups of women examined					p
	all women	M and PMS	M without PMS	NM and PMS	NM without PMS	
n (%)	50 (100)	29 (58)	9 (18)	10 (20)	2 (4)	
Age at the time of examination ($\bar{x} \pm SD$)	36.5 \pm 8.0	35.9 \pm 7.5	39.9 \pm 9.4	35.5 \pm 8.9	34.5 \pm 6.4	0.574
Age at the time of headache onset (years), ($\bar{x} \pm SD$)	20.7 \pm 9.1	21.3 \pm 8.7	19.9 \pm 10.4	18.2 \pm 9.3	27.5 \pm 9.2	0.567
Age at the time of menarche (years), ($\bar{x} \pm SD$)	12.6 \pm 1.2	12.6 \pm 1.2	12.6 \pm 1.1	12.8 \pm 0.9	11.0 \pm 1.4	0.275
Frequency (days in one month), ($\bar{x} \pm SD$)	4.5 \pm 3.8	4.1 \pm 3.1	3.8 \pm 4.3	6.8 \pm 4.7	3.0 \pm 1.4	0.189
Duration of attack (h), ($\bar{x} \pm SD$)	35.7 \pm 27.5	39.9 \pm 27.4	37.9 \pm 32.9	25.8 \pm 22.9	14.0 \pm 14.1	0.360
Education – college and more; n (%)	28 (56.0)	15 (51.7)	5 (55.6)	8 (80.0)	0	0.165
Nulliparous; n (%)	16 (32.0)	11 (37.9)	2 (22.2)	3 (30.0)	0	0.610

M – migraine; NM – non-migraine headache; PMS – premenstrual syndrome; $p < 0.05$ – statistically significant

Table 2
Demographic features and clinical characteristics of headache in women with menstrual migraine

Parameters	Groups of women		p
	pure menstrual migraine	menstrually related migraine	
n (%)	26 (68.4)	12 (31.6)	
Age at the time of examination (years), ($\bar{x} \pm SD$)	38.58 \pm 8.02	33.00 \pm 7.03	0.046
Age at the time of headache onset (years), ($\bar{x} \pm SD$)	22.96 \pm 9.17	16.67 \pm 7.28	0.044
Age at the time of menarche (years), ($\bar{x} \pm SD$)	12.50 \pm 1.175	12.75 \pm 1.29	0.558
Frequency (days in month), ($\bar{x} \pm SD$)	3.35 \pm 2.98	5.42 \pm 3.85	0.078
Duration of attack (h), ($\bar{x} \pm SD$)	39.54 \pm 28.99	39.17 \pm 28.20	0.971
Number of PMS symptoms (0–28), ($\bar{x} \pm SD$)	8.23 \pm 4.57	10.83 \pm 3.90	0.097
Education – college and more n (%)	13 (50.0)	7 (58.3)	0.632
Nulliparous, n (%)	6 (23.1)	7 (58.3)	0.033

PMS – premenstrual syndrome; $p < 0.05$ – statistically significant

Compared with women with menstrually related migraine, women with pure menstrual migraine were older at the time of examination and at the time of headache onset, as well. Age at the time of menarche was similar in all the examined women. Age at the time of headache onset and menarche in women with menstrual migraine is given in Figure 1.

Characteristics of headache (duration of attack and frequency), intensity of PMS and education level were not significantly different in the examined groups, but the percent of women not having children at the time of examination was higher in the group with menstrually related migraine (Table 2).

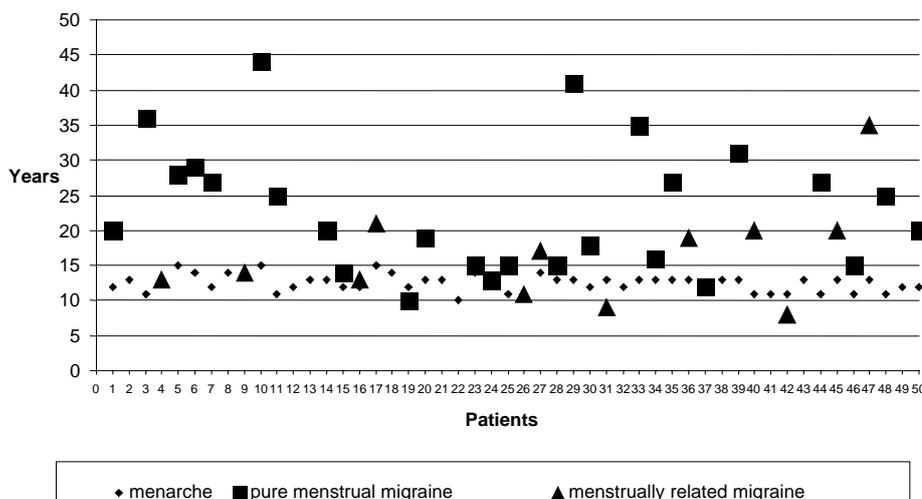


Fig. 1 – Age at the time of headache onset and menarche in women with pure menstrual and menstrually related migraine

Intensity of PMS was not different in the groups of women with different types of headache ($p = 0.184$): total number of PMS symptoms was 8.2 ± 4.6 in the group with pure menstrual migraine, 10.8 ± 3.9 in the group with menstrually related migraine and 10.8 ± 6.3 in the group with non-migraine headache.

Discussion

Since ICHD⁴ does not recognize menstrual migraine as separate entity, the Appendix to ICHD, as a suggestion for the next revision of classification, gives diagnostic criteria for two types of menstrual migraine, pure menstrual and menstrually-related migraine. Diagnoses of specific types of headache in this study were put according to these diagnostic criteria. In the patients with perimenstrual headache which fulfills diagnostic criteria for migraine without aura, more than 60% had pure menstrual, and about one third of them had menstrually related migraine. Results of several studies⁸⁻¹³ suggest that in population of women with migraine without aura, menstrually related migraine has higher frequency of 35% to 54%, and pure menstrual migraine is reported in 4% to 21% cases. Predominance of pure menstrual migraine in our results can be explained by a specific selection of patients in the Headache Center, as a third level health care center. Secondly, using inclusion criteria of having headache in perimenstrual period, we got the results of predominance of pure menstrual migraine in patients with migraine in perimenstrual period, while previous investigation's subject was general population of women with migraine without aura.

The majority of women, two third of them, had migraine without aura, and one third had non-migraine headache. There is no sufficient data indicating that headache occurring in perimenstrual period has to be migraine without aura only. In the last edition of ICHD, only one type of primary headaches is related to perimenstrual period, migraine without aura with its two forms: pure menstrual and menstrually related migraine. Time relation of perimenstrual period and headache attacks in patients with tension type headache and cluster headache has been reported as a result of only few studies^{14, 15}. In this study, women with headache attacks not fulfilling ICHD diagnostic criteria for migraine without aura were classified in the group with non-migraine headache. In that way, non-migraine headache attacks fulfilled ICHD diagnostic criteria for tension type headache, given in the ICHD as a negation of migraine criteria, and the conclusion is that one third of women in this study had, in fact, tension type headache in perimenstrual period. In the study which examined 45 women with headache and PMS,

60% of them had migraine without aura, and about 30% had tension type headache¹⁶. This data are in accordance with suggestions of some authors that menstrual tension type headache exists as a separate entity and because of that deserves its place and definition in ICHD¹⁴.

Most of women with perimenstrual headache had mild PMS. Different types of headache were not related to intensity of PMS, meaning that PMS was not more severe in women with non-migraine headache comparing to those with migraine. Only few studies investigated if some specific type of headache in perimenstrual period is dominant in patients with PMS, so, the contribution of our study is the data that migraine without aura, as the most frequent type of headache in perimenstrual period, is not dependent on intensity of PMS.

Women with pure menstrual migraine, comparing to women with menstrually related migraine, were older at the time of first examination. This data suggests that women with headache occurring not only in the perimenstrual period, but additionally in other time of menstrual cycle, are more disabled by a high frequency of headache attacks, have lower quality of life and contact doctor for help earlier. Also, women with pure menstrual migraine were older at the time of headache onset, while age of menarche was similar in all women. According to the present knowledge, authors of this paper are not able to give explanation for this result. Time gap between age at the time of menarche and age at the time of headache onset in women with menstrual migraine, is not reported by other authors. Hershey¹⁷ reports time relation between first attack of menstrual migraine and menarche, but Kröner-Herwig and Vath¹⁸ do not find a connection between menarche and increased frequency of headache in girls in puberty. There is a lack of explanation for even more significant time gap between menarche and headache onset in women with pure menstrual migraine, comparing to those with menstrually related migraine.

A significantly higher percent of women with pure menstrual migraine already had children at the time of examination, what can be connected to age at the time of first examination.

Conclusion

This study shows that headache occurring in perimenstrual period is not always migraine, but could fulfill diagnostic criteria for tension-type headache, as well. Specific characteristics of perimenstrual headache, which could distinguish it as a symptom of PMS, were not found. An expected relation in time of headache onset and menarche was not confirmed in this study.

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Questionnaire for Headache

Name _____ Number _____

Date of birth: _____

Phone: _____

Education level: primary school / high school / university degree

Profession: _____

Children yes / no, how many children _____

In what way did pregnancy affect migraine _____

Migraine after birth during breastfeeding and after breastfeeding _____

Height _____ cm Weight _____ kg

Right handed / left handed / Ambidexter

Age of headache onset: _____

Age of menstruation onset: _____

Inclusive criteria:

Headache in perimenstrual period in 2 out of 3 menstrual cycles yes / no

Exclusive criteria:

Irregular menstrual cycle yes / no

Hormonal therapy yes / no

Contraceptives yes/no

Prophylactic therapy of migraine yes / no

Pregnancy yes / no

Breastfeeding yes / no

Other acute or chronic disease yes / no

Frequency: _____ days in month**Connection with perimenstrual period:**

Headache occurs _____ days before menstruation (from day 1)

During ovulation yes / no (On what day after day 1 _____)

During menstruation yes / no (On what day after day 1 _____)

After menstruation yes / no (On what day after day 1 _____)

Intensity of pain: _____ on the scale from 0 to 10 (untreated)

WORSENING WITH PHYSICAL ACTIVITY YES / NO

QUALITY OF PAIN: sharp dull pulsating (constant)

LOCALISATION: Unilateral – changing sides,
 Unilateral – without changing sides, Left/right
 Bilateral
 Diffuse

DURATION OF HEADACHE: _____ hours

ACCOMPANING SYMPTOMS:

photo ___%, phono ___%, osmophobia ___%, nausea ___%, vomiting ___% (for each - percent of migraine attacks)

PRODROMS:

hunger/ yawning / tiredness / swelling / lack of mental concentration / mood changes /
other: _____

PROVOCATIVE FACTORS:

Stress / hunger / lack of sleep / too much of sleep / tiredness / type of food / medications /
other: _____

THERAPY:

Acute:

Which medication you usually use for stopping the attack? _____

Prophylactic if tried beforehand: _____

Do you use any kind of medication daily? _____

Other medication (not for headache): _____

HABITS: smoking yes / no , alcohol yes / no, coffee yes / no

FAMILY ANAMNESIS: Does someone from your family suffer from headache yes / no (exact relation to the subject) _____

Are those headaches similar to yours? yes / no

Date: __ / __ / _____

Questionnaire for PMS

- 0 - no symptoms
 1 - mild symptom
 2 - moderate symptom
 3 - severe symptom

SYMPTOM	BEFORE	DURING menstrual bleeding	AFTER
HEADACHE			
LUMBAL PAIN			
TIREDNESS			
NUMBNESS OF THE BODY			
INSOMNIA			
FORGETFULNESS			
CONCENTRATION DIFFICULTIES			
ABSTRACTION			
CLUMSINESS			
WORKING DIFFICULTIES			
FAINTING			
SWEATING			
FREQUENT URINATION			
REDUCE INTEREST IN SEX			
HUNGER FOR SWEETS			
NAUSEA, VOMITING			
WEIGHT GAIN			
BREAST PAIN			
EYELID EDEMA			
CRYING			
DEPRESSION			
MOOD CHANGES			
ENHANCEMENT OF APPETITE			
VISUAL DISTURBANCES			
PALPOTATIONS			
ACNE			
FREQUENT INFECTIONS			
ALERGIC REACTIONS			

NAME

NUMBER

DATE