

ORIGINAL ARTICLE

RELATIONSHIP BETWEEN PATHOLOGICAL MENSTRUAL SYMPTOMS AND THE DEVELOPMENT OF EXTRAGENITAL FORMS OF LOCAL INFLAMMATION

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ABSTRACT

The aim: To evaluate the parameters of menstrual function in 1015 women of reproductive age and to establish the relationship between the detected menstrual disorders and the development of migraine and/or irritable bowel syndrome (IBS).

Materials and methods: During 2018–2020, a survey of women of reproductive age in the Ternopil region (Ukraine) was conducted. To interview the study respondents, we developed a questionnaire that assessed the parameters of menstrual function (age of menarche; regularity and cyclicity of menstrual changes; duration of the menstrual cycle and menstruation itself; the amount of blood loss with the pictogram, the presence of clots and their size) identify characteristic changes in health, symptoms of irritable bowel syndrome and migraine associated with the menstrual cycle. Data analysis was performed by statistical and mathematical method.

Results and conclusions: In 72.2 % of respondents, the study revealed deviations from the normal course of the menstrual cycle. In particular, an increase in blood loss during menstruation and the appearance of clots larger than 1 cm were observed in 40.8 % of women. Among patients with menstrual dysfunction, 51.8 % of patients had symptoms of irritable bowel syndrome, and 44.1 % had signs of migraine.

Thus, the relationship between cyclic menstrual disorders and the formation of IBS and migraine, which significantly affects the deterioration of health, performance of women of childbearing age.

KEY WORDS: menstrual cycle and its features, menstrual inflammation, irritable bowel syndrome (IBS), migraine disorders, women of reproductive age

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INTRODUCTION

In recent years, in the modern medical literature there are frequent data on the relationship between disorders of endometrial regeneration in menstrual cycles and the emergence of inflammatory symptoms in organs with genetically determined or acquired sensitivity to monthly hormonal and immunological changes in the reproductive organs [1, 2].

In particular, the study by Bertone-Johnson E.R., Ronnenberg A.G., Houghton S.C., et al. [3], in patients of reproductive age with manifestations of premenstrual syndrome (PMS) there were pronounced fluctuations in the concentrations of key inflammatory mediators (cytokines – interleukins of the types 8, 6 and 4; matrix metalloproteinase-1; cyclooxygenase-2, prostaglandins PGE2 and PGF2 α , histamine, serotonin, bradykinin, tumor necrosis factor- α) during the cycle compared with women without PMS [4, 5].

According to the works of Heitkemper M.M. et al. and Berbic M., Ng C.H.M., Fraser I.S., who studied immunological changes in patients with normal menstrual function, menstrual inflammation should be considered as a physiological process that occurs in response to interactions between the endocrine and immune systems [6–8]. However, the appearance of symptoms of local and

systemic inflammation in the non-reproductive organs and systems associated with menstruation is the result of a violation of the latter [9, 10, 11].

Thus, further study of the features of the menstrual cycle as a predictor of the development of pathological disorders in organs and systems genetically sensitive to cyclical changes in the body of a woman is relevant.

THE AIM

The aim of the study was to evaluate the parameters of menstrual function in 1015 women of reproductive age and to establish the relationship between the detected menstrual disorders and the development of migraine and/or irritable bowel syndrome.

MATERIALS AND METHODS

The study was conducted on the basis of the Ternopil Regional Clinical Perinatal Center “Mother and Child”, which is the clinical base of the Department of Obstetrics and Gynecology No. 1, Medical Faculty of Ternopil National Medical University.

| No | QUESTION | RESPONSE |
|----|---|--|
| 1 | Your age? | [] [] years |
| 2 | Age when menarche appeared for the first time? | [] [] years |
| 3 | Your menstrual cycle duration? | [] [] days |
| 4 | Your menstruation duration? | [] days |
| 5 | Assess your blood loss volume during menstruation? (choose from the options suggested) | [] A. little; [] B. normal; [] C. significant. |
| 6 | Are there any blood clots in your secretion (more than 1 cm)? | YES NO |
| 7 | Which personal hygiene product do you use? (choose A (sanitary napkin), B (tampon) or C (other) and tick the answer v) [] A. Sanitary napkin 1. How many sanitary napkins do you use a day? [] [] pcs. 2. Day (choose the blood loss volume from the options suggested below): [] [] [] [] 3. How many night sanitary napkins do you use? [] [] pcs. 4. Night (choose the blood loss volume from the options suggested below): [] [] [] [] [] B. Tampon 1. How many tampons do you use during the day? [] [] pcs. 2. Which type of tampons do you use? [] 2 drops ○○ [] 3 drops ○○○ [] 4 drops ○○○○ [] 5 drops ○○○○○ [] 6 drops ○○○○○○ 3. From the options suggested below choose the blood loss volume: [] [] [] [] [] [] [] C. Other Please indicate which hygiene products do you use _____ | |
| 8 | Is your menstrual cycle regular? | YES (menstrual cycle variability ≤ 7-9 days) NO (menstrual cycle variability ≥ 9 days) |
| 9 | Are there any blood clots in your secretion in between the menstruations? | YES [] In the beginning of menstrual cycle [] In the middle of menstrual cycle [] In the end of menstrual cycle [] Non-cyclical NO |
| 10 | Do you have any bad habits? [] alcohol consumption; [] smoking; | YES ← NO |

| SYMPTOMS | | YES | NO |
|----------|--|-------|----|
| 11 | Are there any overall health changes (giddiness, mood alteration, irritability) before menstruation? | YES | NO |
| 12 | Is your working ability decreased before menstruation? | YES | NO |
| 13 | Does pain trouble you in the lower part of abdomen before menstruation? | YES | NO |
| 14 | Are there any overall health changes during menstruation? | YES | NO |
| 15 | Is your working ability decreased during menstruation? | YES | NO |
| 16 | Does pain trouble you in the lower part of abdomen during menstruation? | YES | NO |
| 17 | Did you have the following symptoms during the last three months before and after your menstruation? | | |
| SYMPTOMS | | YES | NO |
| | Recurrent pain or discomfort in the abdominal cavity of 3 days duration? | YES | NO |
| | Flatulence, nausea, vomiting or acid reflux? | YES | NO |
| | Diarrhoea or constipation? | YES | NO |
| | Does pain intensity vary after meals? | YES | NO |
| | Does pain intensity vary or improvement occur after defecation? | YES | NO |
| | Do defecation characteristics change? | YES | NO |
| 18 | Do you have sleeping troubles? | YES | NO |
| 19 | Does headache often trouble you? | YES | NO |
| 20 | Did you have the following symptoms during the last three months before and after your menstruation? | | |
| SYMPTOMS | | YES | NO |
| | Pain lasting for more than 4 hours? (without treatment or with inefficient therapy) | YES | NO |
| | Unilateral pain localization? | YES | NO |
| | Throbbing pain? | YES | NO |
| | Pain intensity from medium to significant? | YES | NO |
| | Nausea and vomiting? | YES | NO |
| | Light and sound intolerance? | YES | NO |
| | Limited workability, ability to study or perform everyday activities for a minimum one day caused by headache? | YES | NO |
| 21 | Do you have any reproductive system diseases? In case YES, please indicate them | YES ← | NO |
| 22 | Do you have any chronic diseases? In case YES, please indicate them | YES ← | NO |

Fig. 1. Sample questionnaire.

| Parameter | Normal | Abnormal | ☑ | |
|---|---|-------------|--------------------------|--------------------------|
| Frequency | Absent (no bleeding) = amenorrhea | | <input type="checkbox"/> | |
| | Infrequent (>38 days) | | <input type="checkbox"/> | |
| | Normal (≥24 to ≤38 days) | | <input type="checkbox"/> | |
| | Frequent (<24 days) | | <input type="checkbox"/> | |
| Duration | Normal (≤8 days) | | <input type="checkbox"/> | |
| | Prolonged (>8 days) | | <input type="checkbox"/> | |
| Regularity | Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)* | | <input type="checkbox"/> | |
| | Irregular (shortest to longest cycle variation: ≥8-10 days)* | | <input type="checkbox"/> | |
| Flow Volume (patient determined) | Light | | <input type="checkbox"/> | |
| | Normal | | <input type="checkbox"/> | |
| | Heavy | | <input type="checkbox"/> | |
| Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses | None | | <input type="checkbox"/> | |
| | Random | | <input type="checkbox"/> | |
| | Cyclic (Predictable) | Early Cycle | | <input type="checkbox"/> |
| | | Mid Cycle | | <input type="checkbox"/> |
| Late Cycle | | | <input type="checkbox"/> | |
| Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections) | Not Applicable (not on gonadal steroid medication) | | <input type="checkbox"/> | |
| | None (on gonadal steroid medication) | | <input type="checkbox"/> | |
| | Present | | <input type="checkbox"/> | |

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Fig. 2. System for determining the parameters of normal menstrual blood loss (FIGO, 2018) [10].

In the period from 2018 to 2020, 1015 women were interviewed. The mean age of patients was (25.2 ± 7.3) years.

To survey the respondents, we developed a questionnaire, which consisted of four blocks of questions. The first block was devoted to assessing the parameters of the menstrual cycle: the time of menarche, regularity and cyclicity, the duration of the cycle and menstruation itself, determining the amount of blood loss, taking into account the amount of hygiene products used day and night and the presence of clots. The presence of bad habits was assessed by question No. 10; changes in health and performance before and during menstruation – questions No. 11–16. The answers of the third and fourth blocks revealed symptoms of irritable bowel syndrome and migraine according to the recommendations of Roman criteria IV and the International Headache Society (Fig. 1) [12, 13, 14].

The assessment of menstrual cycle parameters was performed according to the updated in 2018 international guidelines (clinical guidelines of the National Institute of Health and Quality of Health Care of the United Kingdom (NICE) and the International Federation of Obstetricians and Gynecologists (FIGO)) (Fig. 2) [15]. Severe menstrual bleeding is considered an indicator of menstrual blood loss 80 ml (Clinical protocol for the management of patients with abnormal uterine bleeding, implemented in accordance with the order of the Ministry of Health of Ukraine of April 13, 2016 No. 353) [16].

For the reliability of the evaluation of the obtained data, the study group did not include patients who regularly (for more than 1 month) taking hormonal contraception and women with tumors and inflammatory diseases of the pelvic organs.

Statistical data processing was performed using Microsoft Excel and STATISTICA 12 software.

RESULTS

According to the questionnaire data, in 91.7 % of cases (931 patients) there was a normal duration of the menstrual cycle. A decrease of <24 days was found in 63 women (6.2 %) (average cycle duration (20.2 ± 0.3) days), and an increase over 38 days – in 21 (2.1 %) (with an average cycle duration of (47.8 ± 1.98) days).

Physiological duration of menstruation was diagnosed in 953 study participants, however, 58 women (5.7 %) indicated a duration of less than 4 days, and 4 (0.4 %) – more than 8 days.

Analysis of the menstrual blood self-monitoring pictogram showed an increase in blood loss in 40.1% of patients (407) and a mean volume was (156.9 ± 5.33) ml.

It was noteworthy that among the cases of increased blood loss in 97.8 % of women there was a normal duration of menstruation, and in 90.9 % – the physiological duration of the menstrual cycle.

Underestimation of blood loss during menstruation in the form of blood clots larger than 1 cm was found in 188 patients with normal pictogram data, indicating chronic monthly blood loss outside of physiological.

In 75.6 % of respondents the menstrual cycle was regular, 24.4% – irregular. Intermenstrual bleeding bothered 8.6 % of women.

77 patients reported smoking, 61 – alcohol use, 69 – had both bad habits.

The answers of the participants showed that in most (977 women – 96.3 %) cyclic changes in the body were accompanied by malaise. Most often, patients complained of lower abdominal pain during menstruation, dizziness, mood lability, irritability. These complaints were prevalent in 97.3 % of women with increased blood loss during menstruation according to self-assessment and in 93.1 % of respondents who indicated the presence of clots of 1 cm or more during menstruation.

In the analysis process of the survey results, 47.9 % (486 women) showed manifestations of irritable bowel syndrome (IBS). Among 6 questions of the questionnaire regarding the diagnostic criteria of IBS (according to Roman Criteria IV), the affirmative answer in most cases concerned complaints about changes in the nature of bowel movements (63 %) and changes in pain intensity after defecation (63.6 %). 212 patients (43.6 %) with manifestations of IBS were characterized by complaints of increased menstrual bleeding over 80 ml, and 224 (46.1 %) – the presence of clots on critical days. The combination of symptoms of IBS with dysmenorrhea was observed in 84.2 % of women, with premenstrual syndrome – in 75.5 %.

According to the questionnaire, in 40.3 % of cases (409 women) there were signs of migraine, which were detected in the presence of three positive responses to the questionnaire (recommendations of the International Headache Association). Manifestation of headache symptoms was accompanied by menstrual irregularities: 188 (46 %) women had a blood loss of more than 80 ml; 180 respondents (44 %) of the study indicated the presence of clots larger than 1 cm; in 14 (3.4 %) women – the duration of the cycle ranged from more than 38 days, in 27 (6.6 %) – less than 24 days; 22 patients (5.4 %) indicated a duration of menstruation of less than 4 days, and 9 (2.2 %) – more than 8 days; irregular cycle was noted by 292 women (71.4 %).

In 115 patients with increased blood loss and in 114 cases of blood clots larger than 1 cm during menstruation, manifestations of IBS and/or migraine were detected.

DISCUSSION

According to the results of the study, 65.7 % of women of reproductive age had symptoms of IBS and/or migraine: IBS – in 486 women, migraine – in 409, combined pathology – in 228. Against the background of these symptoms, according to personal data, respondents had certain disorders menstrual cycle: in 78.2 % (370 women) with manifestations of IBS and in 79 % (323 patients) – migraines. The most common menstrual cycle disorders in patients with IBS and migraine were associated with changes in menstrual blood volume parameters (> 80 ml) and/or the appearance of clots larger than 1 cm on menstrual days: in IBS – 319 cases (65.6 %), with migraine – 264 (64.5 %), respectively.

Despite the fact that menstruation is a monthly physiological process of endometrial recovery in non-pregnant women of reproductive age, increasing the duration and intensity of bleeding over time leads to prolongation of local and systemic inflammatory reactions at different levels, which eventually are present in premenstrual syndrome (PMS) to premenstrual magnification.

Given the average age of menarche and the duration of the reproductive period in study respondents and cyclical abnormalities of the menstrual cycle, including increased menstrual blood loss, symptoms of IBS and migraine as manifestations of extragenital local inflammation, may be the result of inadequate restoration of normal cytoarchitecture of endometrial tissue on the background of immunological and hormonal changes.

CONCLUSIONS

1. The frequency of menstrual disorders among women in the study group was observed in 72.2 %. Among the latter, the symptoms of IBS were found in 51.8 %, migraines – in 44.1 %.
2. Among the menstrual cycle disorders in women with IBS most often there was a change in the parameters of menstrual blood volume > 80 ml (43.6 %) and the appearance of clots larger than 1 cm on critical days (46.1 %) and in patients with migraine – 46 % and 44 % respectively.
3. According to the results of the study, cyclic menstrual disorders with a pronounced increase in blood loss during menstruation should be considered as a trigger for the development of IBS and migraine.
4. Given this hypothesis, the management of the diagnosis of IBS and migraine in women of reproductive age should be supplemented by a detailed analysis of menstrual function, and treatment – to include appropriate correction of menstrual cycle disorders.

REFERENCES

1. Antypkin Y.G., Vdovychenko Y.P., Graziottin A. et al. Uterine bleedings and quality of woman's life. *Reprod Endocrinol.* 2019;3(47):13-8.
2. Horban N.Y., Vovk I.B., Lysiana T.O. et al. Peculiarities of uterine cavity biocenosis in patients with different types of endometrial hyperproliferative pathology. *J Med Life.* 2019;12(3):266–70.
3. Bertone-Johnson E.R., Ronnenberg A.G., Houghton S.C. et al. Association of inflammation markers with menstrual symptom severity and premenstrual syndrome in young women. *Hum Reprod.* 2014;29;9:1987–94.
4. Menzies F.M., Shepherd M.C., Nibbs R.J. et al. The role of mast cells and their mediators in reproduction, pregnancy and labour. *Hum Reprod Update.* 2011;17.3:383–96.
5. Barbieri R.L. The endocrinology of the menstrual cycle. *Method Mol Biol.* 2014;1154:145–69.
6. Berbic M., Ng C.H.M., Fraser I.S. Inflammation and endometrial bleeding. *Climacteric* 2014;2(17):47–53.
7. Heitkemper M.M., Cain K.C., Jarrett M.E. et al. Relationship of bloating to other GI and menstrual symptoms in women with irritable bowel syndrome. *Dig Dis Sci.* 2004;49:88–95.
8. Evans J., Salamonsen L.A. Inflammation, leukocytes and menstruation. *Rev Endocr Metab Disor.* 2012;13:277–88.
9. Azlan A., Salamonsen L.A., Hutchison J. Endometrial inflammasome activation accompanies menstruation and may have implications for systemic inflammatory events of the menstrual cycle. *Hum Reprod.* 2020;6(35):1363–76.
10. Nikitina I.M., Smiyan S.A., Kondratiuk K.O. et al. Conditions of microelements exchange processes in women's placentas in intrauterine infection of the fetus. *Wiad. Lek.,* 2020;(7):1434–1438.
11. Martin V.T., Lipton R.B. Epidemiology and biology of menstrual migraine. *Headache.* 2008;3(48):124–30.
12. Nikitina I.N., Boychuk A.V., Babar T. V. et al. Prediction of threats to multiple pregnancy interruption depending on the cause of its occurrence. *Research Journal of Pharmaceutical, Biological and Chemical Sciences.* 2016;7(5):764–771.
13. Malanchuk L., Riabokon M., Malanchuk A. et al. The use of data mining techniques for analysis of menstrual cycle parameters and prognosis of migraine symptoms in reproductive age women. *Advanced computer information technologies.* 2020, p.77–82.
14. Munro M.G., Critchley H.O.D., Fraser I.S. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynecol Obstet.* 2018;143:393–408.
15. Gorban N.E., Vovk I.B., Nikitina I.M. et al. Immunoglobulin indicators to viruses cytomegal and genital herpes in the blood serum of women with non-atypical endometrial hyperproliferative pathology. *Wiad. Lek.* 2020;(8):1600–1605.
16. MoH of Ukraine. Klinichniy protokol z vedennia patsientok iz anomalnyimi matkovymy krvotekhamy, implementovanyi zhidno z nakazom MOZ Ukrainy vid 13.04.2016 r. № 353. [Clinical protocol for the management of patients with abnormal uterine bleeding, implemented in accordance with the Order of the Ministry of Health of Ukraine dated April 13, 2016, No. 353]. (in Ukr.)

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The Authors declare no conflict of interest.

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