The causes of abnormal uterine bleeding in women with chronic psychogenic stress

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article;
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Abnormal uterine bleeding (AUB) is a common pathology in women of reproductive age. Chronic psychogenic stress significantly impacts the parameters of the menstrual cycle and can result in its disorders and AUB.

The aim of the study was to determine the main etiological causes of AUB in women of reproductive age with chronic psychogenic stress.

Materials and methods. We studied the causes of AUB using PALM-COEIN classification in 100 women of reproductive age with chronic psychogenic stress (group I) and 50 patients without chronic psychogenic stress (group II). 30 practically healthy women without AUB and chronic psychogenic stress were the control group.

Results. The most often disorders of menstrual cycle in women in group I were intermenstrual bleeding (IMB) – 38.00 %, prolonged menstrual bleeding – 31.00 %, heavy menstrual bleeding (HMB) – 29.00 %, in group II– HMB (36.00 %), prolonged menstrual bleeding – 34.00 % and IMB – 30.00 %. The most often reasons of AUB in group I were ovulatory dysfunction – 36.00 %, leiomyoma – 24.00 % and adenomyosis – 18.00 %, in group II – leiomyoma – 38.00 %, polyps – 26.00 % and adenomyosis – 20.00 %. In patients of reproductive age, the rate of structural causes for AUB predominated over functional factors but the organic reasons occurred more often in persons without stress factor (80.33 %, P = 0.01) than those in individuals with chronic psychogenic stress (60.71 %). But the frequency of ovulatory dysfunction was 2.57 times more (χ^2 = 6.85, P = 0.009) in persons with chronic psychogenic stress compared to the patients without chronic psychogenic stress (14.00 %).

Conclusions. In patients of reproductive age, the structural causes predominate over non-structural factors in the development of abnormal uterine bleeding. But in women with chronic psychogenic stress, ovulatory dysfunction is the most common reason of AUB.

Причини аномальних маткових кровотеч у жінок в умовах хронічного психоемоційного стресу

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Аномальні маткові кровотечі (АМК) – поширена патологія в жінок репродуктивного віку. Хронічний психоемоційний стрес суттєво впливає на параметри менструального циклу, може призводити до його порушень і виникнення АМК.

Мета роботи – визначити основні етіологічні причини АМК у жінок репродуктивного віку в умовах хронічного психоемоційного стресу.

Матеріали та методи. Вивчили причини АМК за класифікацією PALM-COEIN у 100 жінок репродуктивного віку з хронічним психоемоційним стресом (І група) та 50 пацієнток без хронічного психоемоційного стресу (ІІ група). У контрольну групу залучили 30 практично здорових жінок, у яких не діагностували АМК і хронічний психоемоційний стрес.

Результати. Найчастіші порушення менструального циклу в жінок І групи – міжменструальні кровотечі (ММК) – 38,00 %, тривалі менструальні кровотечі – 31,00 %, тяжкі менструальні кровотечі (ТМК) – 29,00 %; у ІІ групі – ТМК (36,00 %), тривалі менструальні кровотечі – 34,00 %, ММК – 30,00 %. Найчастіші причини АМК у І групі – порушення овуляції (36,00 %), лейоміома (24,00 %), аденоміоз (18,00 %); у ІІ групі – лейоміома (38,00 %), поліпи (26,00 %) та аденоміоз (20,00 %). У пацієнток репродуктивного віку частота структурних причин АМК переважає над функціональними факторами, але органічні чинники частіше виявляли в осіб без стресового фактора (80,33 %, р = 0,01) порівняно з жінками із хронічним психоемоційним стресом (60,71 %). Проте частота овуляційної дисфункції в 2,57 раза вища (χ^2 = 6,85, р = 0,009) в жінок із хронічним психоемоційним стресом порівняно з пацієнтками без нього (14,00 %).

Висновки. У пацієнток репродуктивного віку в розвитку аномальних маткових кровотеч структурні фактори переважають над неструктурними. У жінок із хронічним психоемоційним стресом овуляторна дисфункція є найчастішою причиною АМК.

The prevalence of abnormal uterine bleeding (AUB) in reproductive age women is approximately 30 % [1]. AUB negatively impacts quality of life in women, including work and education [2,3]. The PALM-COEIN classification presents the main etiological factors of AUB [4]. The management of AUB is successful due to the introduction of new diagnostic and therapeutic approaches and guidelines, which were proposed in 2011 by the International Federation of Obstetricians and Gynecologists and updated in 2018 [1,4]. However, social factors are vital and significantly impact a woman's health.

Among such factors, special attention should be paid to stress, the mechanisms of which significantly influence

the menstrual function and lead to its disorders [5,6]. Psychogenic stress conditions substantially affect the menstrual cycle. Stress factors can result in hyperprolactinemia, anovulation, amenorrhea, AUB, infertility, etc. [7,8]. Also, it was found that psychosocial stress can cause irregular menstrual cycle and be associated with premenstrual syndrome [9], secondary dysmenorrhea [10], etc.

Nowadays, there are a large number of scientific publications and clinical protocols for the diagnosis and treatment of AUB but only single literary manuscripts are focused on the study of stress factors in the pathology genesis. Thus, there is a necessity in the complex knowledge of understanding the deep pathogenetic mechanisms of AUB in women of reproductive age with chronic psychogenic stress, which will allow to propose an individual approach to their treatment.

Aim

The aim of the study was to determine the main etiological causes of AUB in women of reproductive age with chronic psychogenic stress.

Materials and methods

100 women with AUB and chronic psychogenic stress formed group I. Group II consisted of 50 women with AUB and without chronic psychogenic stress. 30 practically healthy women without AUB and chronic stress were the control group.

Inclusion criteria: age 18–45 years old, AUB, satisfactory specimen from the uterine cavity for histological study, patient consent. Exclusion criteria: pregnancy, acute inflammatory diseases of female genitalia, blood pathology with coagulation disorders, mental diseases, hypothyroidism, hyperthyroid conditions.

The diagnosis of AUB, chronic and acute AUB, heavy menstrual bleeding (HMB), intermenstrual bleeding (IMB) and etiological causes were based on the FIGO's recommendations [4]. Chronic psychogenic stress was diagnosed by a clinical interview with a psychologist [11,12]. Stress level was assessed by the Perceived Stress Scale-10 (PSS-10) [13,14].

The study was conducted in Kreminna multidisciplinary hospital of Kreminna district council (Ukraine) and confirmed by the Ethics commission (protocol No. 1, 15.01.2018) in Shupyk Healthcare National Medical University of Ukraine following by the ethical standards of the Declaration of Helsinki (1964).

We used the program Statistica 6.0 to process statistical data – the parameters of descriptive statistics (mean, standard error of the mean), and the criterion χ^2 (Yates corrected Chi-square) was used to compare the data between groups.

Results

The mean age of the women in groups I (31.09 ± 0.60 years) and II (33.06 ± 0.91 years) was significantly higher (P < 0.001) than that in the control one (26.33 ± 0.87 years). It occurred due to a less number of individuals aged 18–24 years in groups I (8 (8.00 %) patients) and II (5 (10.00 %) patients) by 4.58 (χ^2 = 12.99, P < 0.001)

and 3.67 times (χ^2 = 76.75, P = 0.009), respectively, relative to the controls (11 (36.67 %) women), and a large number of individuals aged 41–45 years (by 3.00 and 3.60 times, respectively, – 20 (20.00 %), 12 (24.44 %) and 2 (6.66 %) persons).

There were no differences in the distribution of women in all groups according to the place of residence and family status. A majority of women lived in cities (67 (67.00 %) persons in group I, 33 (66.00 %) – II, 17 (56.67 %) – control one) than in rural area (33 (33.00 %), 17 (34.00 %) and 13 (43.33 %) individuals, respectively). The number of officially married women dominated (90 (90.00 %), 39 (78.00 %) and 28 (93.33 %) women).

The mean of body mass index was similar in all groups – 24.37 ± 0.34 kg/m^2 in group I, 23.89 ± 0.43 kg/m^2 – in group II and 23.69 ± 0.47 kg/m^2 – in the control one.

The level of perceived stress, assessed on the PSS-10 scale, in patients with AUB and chronic stress (32.24 ± 0.44) was 1.97 times increased relative to healthy women (16.33 ± 0.64, P < 0.001), and 1.12 times – to patients with AUB without chronic stress (18.24 ± 0.66).

The mean age at menarche in women with AUB and chronic psychogenic stress was 12.72 ± 0.11 years old, which coincided with that in patients with AUB without chronic psychogenic stress (12.74 ± 0.15 years) and healthy subjects (12.40 ± 0.25 years).

According to the structure of gynecological pathology, significant differences were found between healthy women and patients with AUB in relation to some diseases (*Table 1*). Thus, the prevalence of leiomyoma among patients in group I was 7.21 times more compared to the control group (χ^2 = 5.08, P = 0.02), in group II – 10.81 times (χ^2 = 9.32, P = 0.002), endometriosis – 3.15 and 3.30 times, respectively, premenstrual syndrome – 3.42 (χ^2 = 13.48, P < 0.001) and 1.56 times, respectively. Algo- / dysmenorrhea was diagnosed in women with AUB and chronic psychogenic stress by 1.86 (χ^2 = 4.51, P = 0.03) and 4.10 times (χ^2 = 8.57, P = 0.003) more often, than that in patients with AUB without chronic stress and healthy individuals.

More than half of the women in all groups had higher education – 69 (69.00 %) in group I, 29 (58.00 %) – II, 16 (53.34 %) – control one. Although there was a greater number of patients with AUB and chronic psychogenic stress who had higher education than in other groups, no significant difference in the level of education between women in different groups was found.

By type of employment, most women with chronic psychogenic stress and AUB worked at schools, colleges, universities (education workers), were physicians/medical nurses, officials, bank employees. However, the quantity of patients engaged in intellectual activity (education workers – teachers/assistants of different educational establishments, physicians/nurses, bank employees, officials, accountants, students, journalists) in group I (86 (86.00 %) individuals) was 1.43 times more than that in group II (30 (60.00 %) women; χ^2 = 11.41, P < 0.001) and 1.36 – compared to the control (19 (63.33 %) persons; χ^2 = 6.24, P = 0.01).

Besides this, in group I, 34 (34.00 %) women held senior positions in work employment versus 5 (10.00 %; χ^2 = 8.77, P = 0.003) and 2 (6.67 %; χ^2 = 7.30, P = 0.007) individuals in groups II and control, respectively. Most of

Table 1. Gynecological pathology and obstetrical history of the patients with AUB

Parameter	Group I (n = 100)		Group II (n = 50)		Control group (n = 30)	
	Abs.	%	Abs.	%	Abs.	%
Chronic salpingitis and oophoritis	24	24.00	10	20.00	5	16.67
Leiomyoma	24	24.00*	18	36.00*	1	3.33
Ovary cyst	16	16.00	5	10.00	1	3.33
Endometriosis	21	21.00	11	22.00	2	6.67
Premenstrual syndrome	57	57.00*°	13	26.00	5	16.67
Algo-/dysmenorrhea	41	41.00*°	11	22.00	3	10.00
Polycystic ovary syndrome	3	3.00	1	2.00	–	–
Infertility	2	2.00	2	4.00	–	–
History of pregnancy	86	86.00	45	90.00	26	86.67
History of labor	84	84.00	43	86.00	26	86.67

*: significant difference between indicators compared to the control group (P < 0.05); **°:** significant difference between indicators of groups I and II (P < 0.05).

Table 2. The clinical parameters of menstrual cycle in patients with AUB

Clinical parameter of the menstrual cycle	Group I (n = 100)		Group II (n = 50)	
	Abs.	%	Abs.	%
Frequency of menstruation				
Normal	69	69.00	37	74.00
Frequent	27	27.00	13	26.00
Infrequent	4	4.00	–	–
Duration of menstrual bleeding				
Normal	69	69.00	33	66.00
Prolonged	31	31.00	17	34.00
Regular menstrual cycle	74	74.00	39	78.00
Irregular menstrual cycle	26	26.00	11	22.00
Volume of menstrual blood loss				
Normal	66	66.00	29	58.00
Light	5	5.00	3	6.00
Heavy	29	29.00	18	36.00
Intermenstrual bleeding, total	38	38.00	15	30.00
Irregular	5	5.00	4	8.00
Cyclic	33	33.00	11	12.00
Unscheduled bleeding with progestin, estrogen, gonadal steroids	8	8.00	1	2.00

Table 3. PALM-COEIN causes of abnormal uterine bleeding in patients with AUB

Cause	Group I (n = 100)		Group II (n = 50)	
	Abs.	%	Abs.	%
Polyp	12	12.00	13	26.00
Adenomyosis	18	18.00	10	20.00
Leiomyoma	24	24.00	19	38.00
Malignancy/hyperplasia	14	14.00	7	14.00
Ovulatory dysfunction	36*	36.00	7	14.00
Endometrial factor	8	8.00	5	10.00

*: significant difference between indicators compared to the control group (P < 0.05).

the persons in all groups were engaged in full-time work – 74 (74.00 %) patients with AUB and chronic psychogenic stress, and 31 (62.00 %) persons with AUB and without psychogenic stress, and 19 (63.34 %) healthy subjects. The number of women who regularly worked overtime (additional other type of work or additional work at the main place of employment) in group I ((23.00 %) individuals) was 2.87 (χ^2 = 4.12, P = 0.02) and 6.91 (χ^2 = 4.69, P = 0.03) times higher compared to groups II (4 (8.00 %)) and control ((1 (3.33 %), respectively. The prevalence of women

who were partially employed was lower in group I – by 10.00 (χ^2 = 20.53, P < 0.001) and 11.00 times (χ^2 = 20.34, P < 0.001), respectively, compared to groups II and control (3 (3.00 %), 15 (30.00 %) and 10 (33.33 %)).

The number of persons with imbalanced working regime and insufficient rest was 1.81 times higher in the group with AUB and chronic psychogenic stress (76 (76.00 %) individuals; χ^2 = 15.41, P < 0.001) than that in the group with AUB and without chronic psychogenic stress (21 (42.00 %)) and by 2.85 times – compared to the control group (8 (26.67 %); χ^2 = 22.45, P < 0.001). Regular night work had 14 (14.00 %) patients in group I versus 2 (4.00 %) in group II, and there were no such persons in the control group.

The prevalence of patients who smoked was 1.64 times higher among patients with AUB and chronic psychogenic stress (36 (36.00 %) persons), than that among AUB patients without chronic psychogenic stress (11 (22.00 %)), and 2.70 times higher than that among healthy women (4 (13.33 %); χ^2 = 4.55, P = 0.03).

Over a third of group I women had to miss their work or study because of AUB during the last year that was 2.25 times more compared to group II (36 (36.00 %) and 8 (16.00 %) individuals, respectively).

Most of the patients in groups I and II had chronic AUB – 92 (92.00 %) and 47 (94.00 %) persons, respectively, acute bleeding – 8 (8.00 %) and 3 (6.00 %), HMB was diagnosed in 29 (29.00 %) and 18 (36.00 %) women. The clinical parameters of menstrual cycle disorders are presented in *Table 2*.

The results of gynecological and clinical examinations, ultrasound sonography of pelvic organs, hysteroscopy and histological study of the material from the uterus cavity demonstrated that the rate of structural causes (PALM) dominated over non-structural reasons (COEIN) in both groups with AUB (*Table 3*).

12 (12.00 %) patients in group I and 11 (22.00 %) persons in group II had two PALM-factors of AUB. Thus, the total number of the structural causes in group I was 112, in group II – 61. So, the ratio of PALM-to-COEIN causes in group I was 68 (60.71 %) to 44 (39.29 %) cases, in group II – 49 (80.33 %) to 12 (19.67 %) cases, so, the frequency of organic factors was significantly higher in group II compared to group I (χ^2 = 6.07, P = 0.01). The most often reasons of AUB in group I were ovulatory dysfunction (36.00 %), leiomyoma (24.00 %) and adenomyosis (18.00 %), in group II – leiomyoma (38.00 %), polyps (26.00 %) and adenomyosis (20.00 %). Attention should be paid to a significant difference in the rate of ovulatory dysfunction between groups. In group I, the number of such cases occurred 2.57 times higher than that in group II (χ^2 = 6.85, P = 0.009).

There was no significant difference in all the above-mentioned social parameters, data of gynecological anamnesis, obstetrical history, type of employment between the patients with acute and chronic AUB in groups I and II. All the women with acute AUB in groups I and II were diagnosed with structural factors of the pathology – leiomyoma and endometrial hyperplasia and there were no functional reasons. Thus, the rate of ovulatory dysfunction cases in the persons with chronic AUB and psychogenic stress was 39.13 % (36 individuals) that was 2,63 times more (χ^2 = 7.45, P = 0.006) than that in the patients without stress – 14.89 % (7 women).

32 ISSN 2306-4145 http://zmj.zsmu.edu.ua

Zaporozhye medical journal. Volume 25. No. 1, January – February 2023

Discussion

According to studies by K. Yamamoto et al., 63.6 % of female students with psychosocial stress had heavy menstruation bleeding, 2.3 % – amenorrhea, 79.2 % – premenstrual syndrome, 62.9 % – irregular menstrual cycle, 2.3 % – duration of menstrual bleeding more than 8 days, 79.2 % – menstrual pain, 5.9 % – menstrual cycle less 24 days, 2.3 % – more than 39 days [9]. Patients in reproductive age with stressful working conditions (medical nurses with night shifts) reported about irregular menstrual cycle at 24.8–35.9 %, the prevalence of AUB (menstrual bleeding more than 8 days) was in 7.2 % of persons, irregular menstrual cycle – 30.3 % [15]. In our study we have found that the most common disorders of menstrual cycle in women of reproductive age with psychogenic stress were IMB (38.00 %), prolonged bleeding (31.00 %), HMB (29.00 %), in patients without stress – HMB (36.00 %), prolonged menstrual bleeding (34.00 %) and IMB (30.00 %).

Structural causes of AUB prevail over non-structural factors. In our study, we observed the similar trend – the total number of structural reasons was more than non-structural ones in both women with chronic psychogenic stress and persons without psychogenic stress. Leiomyoma is the most common cause of AUB in women of reproductive age [16]. It occurs in 44.5 % cases of AUB [17]. The ranges of its frequency based on different researches are 30 % [18] – 53.7 % [19]. Endometrial hyperplasia is also a common reason of menstrual disorders in women [20]. In our study, leiomyoma was also the most often cause of AUB in patients without psychogenic stress – 36.00 %, but in persons with psychogenic stress, ovulatory dysfunction was the most common cause of AUB (36.00 %) and the frequency of leiomyoma was 24.00 %.

Stress significantly influences different organs and systems of the organism through the activation of hypothalamic-pituitary-adrenal system, release of adrenocorticotropic hormone which stimulates cortisol secretion [5]. High cortisol concentrations lead to a decrease in gonadotropin releasing hormone, which stimulates the synthesis, secretion and release of follicle-stimulating hormone and luteinizing hormone, so, their levels become less. Stress also stimulates serotonin which increases prolactin concentrations. High prolactin level and insufficiency of follicle-stimulating hormone and luteinizing hormone contribute to ovulatory disorders, anovulation, luteal phase insufficiency, infertility, etc. [5]. So, the results of our study have confirmed these data and demonstrated that in women with chronic psychogenic stress, ovulatory dysfunction was the most relevant reason for AUB.

Conclusions

1. In patients of reproductive age, the rate of structural causes of abnormal uterine bleeding predominates over functional factors but the organic reasons occur more often in persons without stress factor (80.33 %, P = 0.01) than those in individuals with chronic psychogenic stress (60.71 %).

2. In women of reproductive age with chronic psychogenic stress, ovulatory dysfunction is the most common reason of abnormal uterine bleeding which occurs in more than one third of cases (36.00 %) and the rate of which

is 2.57 times higher (P < 0.05) compared to the persons without stress factor.

Prospects for the further research. It seems perspective to perform a detailed analysis of hormonal disorders in patients with abnormal uterine bleeding and chronic psychogenic stress.

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Zaporozhye medical journal. Volume 25. No. 1, January – February 2023