NEW PATTERNS OF MENSTRUAL DISORDERS' TREATMENT – UNIFICATION OF THE METHOD

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O.V. GRYSHCHENKO
MD, professor, head of the Perinatology, Obstetrics and Gynecology Department, Kharkiv Medical Academy of Postgraduate Education
ORCID: 0000-0002-2410-861X

V.V. BOBRYTSKA
PhD, associate professor at the Perinatology, Obstetrics and Gynecology Department, Kharkiv Medical Academy of Postgraduate Education
ORCID:0000-0002-7816-6575

Contacts:
Victoria V. Bobrytska
Kharkiv Medical Academy of Postgraduate Education, Perinatology, Obstetrics and Gynecology Department
Amosova str. 58
61176, Kharkiv, Ukraine
Tel.: +38 (057) 711 95 42
email: bobritska@gmail.com

INTRODUCTION

Menstrual cycle (MC) disorders is one of the most common pathological conditions and unites pathogenetically various diseases that manifest a violation of the duration, frequency of menstruation, the amount of menstrual flow [4, 9, 10].

The variety of manifestations of the menstrual disorders combine similar stages of pathogenesis and often similar treatment regimens. However, today given the abundance and variety of medicines, homeopathic and herbal remedies of various types of producing and application forms it becomes difficult to determine the optimal preparation, as well as to avoid polypharmacy, which is so typical of modern medicine.

The search for optimal means and medicines for the treatment of various types of MC disorders, comparison of efficiency, compliance, the absence of significant side effects is the task of conducting clinical researching [11, 13].

ANALYSIS OF LITERATURE DATA AND STATEMENT OF RESEARCH PROBLEM

The concept of menstrual disorders combines a large range of pathological conditions and diseases, clearly defined by the International Classification of Diseases ICD-10 [1]. Various nosological forms of the menstrual disorders are represented by sections N91.0-91.5 (the abbreviation NOS is no other (additional) specifications):

- **N91 Absent, scanty and rare menstruation**

Excludes ovarian dysfunction (E28)

o N91.0 Primary amenorrhea

Failed menstruation at puberty.

o N91.1 Secondary amenorrhea

The absence of menstruation in women who previously had them (loss of menstrual period).

o N91.2 Amenorrhea, unspecified

Absence of menstruation, NOS.

o N91.3 Primary oligomenorrhea

Scanty or rare menstruation since their onset

o N91.4 Secondary oligomenorrhea

Scanty or rare menstruation in women with previously normal menstruation.

o N91.5 Oligomenorrhea, unspecified

Hypomenorrhea, NOS.

- **N92 Excessive, frequent and irregular menstruation**

Excludes: postmenopausal bleeding (N95.0); precocious puberty (menstruation) (E30.0)

o N92.0 Abundant and frequent menstruation with a regular cycle

Periodically heavy menstruation NOS. Menorrhagia NOS. Polymenorrhea. Spots, spotting intermenstrual (regular).

o N92.1 Abundant and frequent menstruation with an irregular cycle

Irregular bleeding in the intermenstrual period. Irregular, shortened menstrual interval bleeding. Menometrorrhagia. Metrorrhagia.

o N92.2 Heavy menstruations during puberty

Heavy bleeding at the beginning of the menstrual period.

Puberty menorrhagia. Puberty bleeding.

o N92.3 Ovulatory bleeding

Regular menstrual bleeding.

o N92.4 Heavy bleeding in the premenopausal period

Menorrhagia or metrorrhagia: climacteric. In menopause.

Premenopausal. In premenopause.

o N92.5 Other specified forms of irregular menstruation

o N92.6 Irregular menstruation, unspecified

The impressive is the abundance of various formulations and types of menstrual cycle disorders presented in the ICD-10. First of all, it is necessary to recollect the definition of the normal duration of the menstrual period. Normal menstruation is considered to be monthly bleeding lasting from 3 to 7 days, with an intermenstrual period of at least 21 days, and a maximum of 35 days [16].

To narrow the spectrum of the search for optimal treatment for menstrual cycle disorders, we selected violations, which are characteristic for the reproductive age, given the fact that many of the drugs used to treat patients of this age period are also applicable in puberty (in the absence of age-related contraindications) [11, 16], and in the premenopausal period [8, 9]. This is first of all herbal products.

Currently, we are observing a rather high percentage of somatic and endocrinological pathologies, which in some cases is a contraindication to hormonal treatment. Fear of hormonal drugs and existing myths about side effects, addiction significantly reduce the possibility of using this pathogenetically substantiated method, and again return to the search for effective herbal remedies.

In addition, one of the theories of the development of menstrual irregularities is an inflammatory process, which results in the formation of ovarian dysfunction, endometrial hyperplasia, and the direct and inverse association between

the central and peripheral links of hormonal homeostasis is violated [2, 7, 9, 10].

Stress is both emotional and physical, is now recognized as one of the reasons, and in some cases the only cause of menstrual disorders. Even excessive exercise, with the goal of general health and endurance, has the opposite "side of the coin" – hypomenstrual syndrome, violation of the menstruation regularity [11, 13].

No denying the positive therapeutic effect of hormonal therapy, and also taking into account the above points of the subjective attitude of patients to this type of treatment specialists from various countries continue to search and perform clinical studies of non-hormonal drugs, mainly herbal composition (which is recognized by many patients as a more "natural" treatment). Aromatherapy studies have been conducted to reduce the symptoms of premenstrual headache, dysmenorrhea [17]. The positive effects of complex herbal remedies recommended as an independent means of treating menstrual irregularities are described [6, 9, 19, 21]. Such drugs, however, should have a hormone-normalizing effect, and also given the above theory of inflammatory genesis an anti-inflammatory effect [2, 21].

One of the often mentioned in foreign and domestic literature is a drug-derivative *Vitex agnus-castus* [4, 6, 7, 18]. The preparation is used to normalize the MC, including accompanied by mastalgia of various origins. Used in various age periods, efficacy and low toxicity are recognized as a result of various clinical studies [3, 5, 6]. The principle of the preparation is the regulation of the neuroendocrine component of the ovarian-menstrual cycle, a decrease in prolactin levels due to dopaminergic action.

The medicine is recognized as clinically effective; however, the mechanism of action does not cover all possible links in the pathogenesis of menstrual cycle disorders. Therefore, it is logical to search and use a complex-acting preparation, including anti-inflammatory, decongestant, normalizing the level of other steroid hormones: cortisol, estrogen ratio of fractions and estrogen/progesterone ratio.

The pride of modern pharmacy without a doubt is a complex herbal product that meets all the above properties, demonstrating high efficiency in a wide variety of clinical situations – Tazalok™. This is a drug that has no analogues in composition, with proven efficacy during the experiment and clinical studies [3]. The clinical effect of the drug in cases of polycystic ovary syndrome, treatment of functional ovarian cysts, endometrial hyperplasia, hypomenstrual syndrome against thyroid diseases has been convincingly proven [4, 6, 7]. The preparation contains tincture of a mixture of medicinal plant material (1:10): six-petalled meadowsweet roots (*Filipendula vulgaris Moench*) – 0.28 g, fresh parsley roots (*Petroselini radix*) – 0.225 g, fresh celery roots (Apiumi radix) – 0.17 g, herbs of the lady's bedstraw (*Galium verum L.*) – 0.135 g, plain flax herbs (*Linariae herba*) – 0.11 g, marigold flowers (*Flores Calendulae*) – 0.08 g (extractant 40% ethanol). Tis drug has practically no contraindications, except for individual sensitivity to the components. The properties are determined by the qualities of the constituents – normalize the estrogen-progesterone ratio, anti-inflammatory, regulating apoptosis and angiogenesis, with anti-inflammatory effect.

Therefore we chose Tazalok™ to conduct a study of clinical efficacy in various types of menstrual disorders, in comparison with a drug derived from *Vitex agnus-castus* (as a monocomponent medicine with a neuroendocrine mechanism of action).

Objective of the study was to optimize the treatment of menstrual irregularities using herbal monotherapy, by comparing the clinical efficacy of Tazalok™ and *Vitex agnus-castus* drug.

MATERIALS AND METHODS

Under observation were 60 patients 23–37 years aged with various forms of menstrual disorders, randomized in two equal groups 30 women according to the group therapy. Patients I (main) groups received for the treatment of menstrual cycle disorders preparation Tazalok™, group II patients (comparison group) – *Vitex agnus-castus* drug.

Considering the variety of menstrual disorders forms we selected patients with two variants of cycle disorders: abundant menstruation and hypomenstrual syndrome.

The main group and the comparison group were divided into two subgroups of 15 patients in accordance with peculiarities of the menstrual disorders. Subgroup IA of the main group – patients with heavy bloody flooding in the menstrual period, IB – patients with scanty menstruation. The comparison group: IIA – heavy menstrual bleeding, IIB – meager menstrual bleeding.

We selected patients with pathological states that match the following ciphers according to ICD-10: N92.0 Abundant and frequent menstruation during regular MC: Periodically heavy menstruation NOS. Menorrhagia NOS. Polymenorrhea; N92.1 Abundant and frequent menstruation with irregular MC: irregular intermenstrual bleeding period. Irregular, shortened menstrual intervals bleeding. Menometrorrhagia. Metrorrhagia; as well as patients with meager menstruation with different MC characteristics; N91.4 Secondary oligomenorrhea: lean or rare menstruation in women with previously normal menstruation; N91.5 Oligomenorrhea, unspecified. Hypomenorrhea NOS.

Insofar as the preparation Tazalok™ is available in the form of oral drops, then in the comparison group we used the *Vitex agnus-castus* drug in solution form (oral drops). In accordance with the instructions for use Tazalok™ was taken in 30 drops 3 times a day or daily dose is divided into two doses. Patients considered more convenient (taking into account active socialization – studying at a university, working with a full schedule) taking drug 2 times a day, 45 drops each. The medicine was taken before meals, dissolving in 100 ml of water. *Vitex agnus-castus* drug was taken in accordance with the instructions for use – 40 drops 1 time a day before meals, also with 100–150 ml of pure water. Both remedies were taken daily without interruption for 3 months.

The study took into account complaints of patients before treatment, during treatment, and also after 3 months of the course, including a subjective assessment of drug tolerance, the presence of side effects with prolonged application.

In order to objectively evaluate the effectiveness of treatment, a standard hormonal study by enzyme-linked immunosorbent assay (ELISA) was performed before therapy and after 3 months of treatment. Investigated of estradiol (E) level, follicle-stimulating hormone (FSH), luteinizing hormone (LH),

progesterone (PG), prolactin (PrL), cortisol (C); thyroid hormones: thyroid-stimulating hormone, free triiodothyronine, thyroxine free, thyroid peroxidase antibodies. All patients underwent general clinical blood tests, analysis of vaginal discharge, PAP-test.

Before and after the end of therapy (3 months later) and according to the indications (if there are complaints) all patients underwent pelvic ultrasound and blood flow in color Doppler using a 3.5 MHz transvaginal sensor. Ultrasound of the mammary glands, thyroid gland was performed with a linear 5 MHz probe (Toshiba Aplio 300).

Intensity of the pain syndrome (mastalgia, dysmenorrhea) was evaluated using the traditional visual-analogue pain scale (VAS) in points: no pain – 0 points, weak pain – 1-2 points, moderate – 3-6 points, severe – 7-9, unbearable – 10 points.

Data obtained during the study were processed by the method of variation statistics using the standard program Statistica 6.0. Confidence level differences were taken as $p < 0.05$.

RESEARCH RESULTS AND DISCUSSION

Patients of both observation groups at the beginning of the study complained of MC disorders (according to subgroups). In addition, complaints of dyspareunia, decreased libido, and depressive mood disorders were characteristic. The frequency of complaints according to the groups and nature of the MC disorders is presented in table 1.

Noteworthy is the higher incidence of dysmenorrhea (painful periods) among patients with heavy menstruation compared with patients with hypomenstrual syndrome. Mastalgia on the eve of menstruation was observed mainly in patients with metrorrhagia, during MC moderate pain in the breast, tingling sensation was noted in 8 patients (53.3%) of IA subgroup and 9 (60.0%) IIA subgroup ($p > 0.05$).

Dysmenorrhea pain was rated as moderate at 5–6 points on the VAS scale for 5 patients from subgroup IA (33.3%), 4 patients from subgroup IIA (26.6%); moderate in 3-4 points – 1 patient of subgroup IA (6.7%), 1 patient of subgroup IIA (6.7%). As mild and moderate pain, the degree of pain of the patient of subgroups IB and IIB was evaluated at 2-3 points – 1 patient (6.7%) in each of these subgroups.

Mastalgia was rated moderate in 4–5 points in 4 (26.6%) patients of subgroup IA, 5 (33.3%) of patients in subgroup IIA. Moderate at 3 points on the VAS scale was pain in 4 (26.6%) patients of subgroup IA and 4 (26.6%) of subgroup IIA. A mild pain syndrome of 2 points was observed in 3 (20.0%) patients of subgroup IB and 2 (13.3%) of subgroup IIB.

Social maladaptation, limitation of physical activity was noted by patients with polymenorrhea. Dyspareunia, decreased libido was characteristic for patients of both examined groups, without statistically significant differences between the groups, which, apparently is the result of hormonal imbalance.

An increased number of transparent mucous vaginal discharge was noted mainly by patients of IB and IIB subgroups, which can also be a sign of hormonal disorders or transferred (chronic) infections.

Gynecological history was burdened in patients of both groups: 5 (33.3%) patients of subgroup IA and 3 (20.0%) of patients of subgroup IB and 4 (26.6%) of patients of subgroups IIA and IIB had salpingoophoritis in remission. 2 (13.3%) patients of subgroup IA and 1 (6.7%) of subgroup IB, 3 (20.0%) women of subgroup IIA and 2 (13.3%) IIB underwent treatment for cervical dysplasia (diathermoconization).

Noteworthy low parity in both observation groups: 1 birth was in 6 patients of the subgroup IA, 4 (26.6%) patients of subgroup IB, 4 (26.6%) patients of subgroup IIA and 3 (20.0%) patients of subgroup IIB ($p > 0.05$). Artificial abortions in early gestations had 2 (13.3%) patients of subgroup IA, 1 (6.7%) of patients of subgroup IB and 2 (13.3%) in subgroup IIB.

Among the data of somatic history, the presence of pathology characteristic of connective tissue dysplasia is noteworthy: varicose veins, mild and moderate myopia, and the presence of striae on the body. Moreover, this pathology was observed significantly more frequently in women with heavy menstruation - in subgroups IA and IIA (table 2).

Endocrinological pathology was represented by thyroid dysfunction, mainly with signs of hypothyroidism – in 7 (46.6%) patients of subgroup IA, 9 (60.0%) of subgroup IB, 8 (53.3%) of IIA and 7 (46.6%) of IIB. Hyperthyroidism was observed in 1 (6.6%) patient of subgroup IB and 2 (13.3%) of subgroup IIB. Autoimmune thyroiditis was detected in 2 (13.3%) patients of subgroup IA, 4 (26.6%) of subgroup IB, 3 (20.0%) subgroups IIA and 3 (20.0%) subgroups IIB ($p > 0.05$). From the data obtained, it can be judged that the presence of hypothyroidism in our study was more characteristic of the clinical course of menstrual disorders with heavy menstrual bleeding – both regular and irregular ($p < 0.05$).

The most indicative are the data from a study of female sex hormones: before the start of therapy, the levels of FSH, LH, and PG were significantly reduced in most patients of both observation groups, an increase in cortisol was noted (table 3). The data obtained are presented in accordance with the follicular and luteal phases of the MC before (table 3, table 5) and after therapy (table 4, table 6).

There was a statistically significant difference in the levels of PrL in the subgroups IA and IIA, IB and IIB, i.e. patients with menstrual cycle disorders, characterized by meager, including irregular menstruation, there is a higher level of PrL. The data presented also show that the level of

Table 1. Nature of complaints of patients of the examined groups before starting therapy, abs. number (%)

Nature of complaints	Subgroups			
	IA (n=15)	IB (n=15)	IIA (n=15)	IIB (n=15)
Dysmenorrhea	6 (40.0)[1]	1 (6.7)[1]	5 (33.3)[2]	1 (6.7)[2]
Dyspareunia	7 (46.6)[3]	9 (60.0)[3]	7 (46.6)[3]	5 (33.3)[3]
Decreased libido	5 (33.3)[3]	6 (40.0)[3]	4 (26.6)[3]	7 (46.6)[3]
Mastalgia	8 (53.3)[1]	3 (20.0)[1]	9 (60.0)[2]	2 (13.3)[2]
Discharge	1 (6.7)[1]	5 (33.3)[1]	2 (13.3)[2]	4 (26.6)[2]
Social maladaptation	6 (40.0)[1]	1 (6.7)[1]	7 (46.6)[2]	1 (6.7)[2]

[1] statistically significant differences between patients IA and IIA subgroups, $p < 0.05$
[2] statistically significant differences between patients IB and IIB subgroups, $p < 0.05$
[3] no statistically significant differences between groups, $p > 0.05$

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Table 2. Frequency of signs of undifferentiated connective tissue dysplasia among patients of the examined groups, abs. number (%)

Signs of connective tissue dysplasia	Subgroups			
	IA (n = 15)	IB (n = 15)	IIA (n = 15)	IIB (n = 15)
Myopia	7 (46.6)	3 (20.0)	8 (53.3)	3 (20.0)
Varicose veins	9 (60.0)	4 (26.6)	10 (66.6)	3 (20.0)
Striae	6 (40.0)	-	5 (33.3)	1 (6.6)
Joint hypermobility	6 (40.0)	-	4 (26.6)	1 (6.6)
Asthenic syndrome	5 (33.3)	1 (6.6)	6 (40.0)	1 (6.6)

Table 3. Levels of sex steroid hormones before therapy in patients of the observation groups, follicular phase of MC

Hormone indicators	Subgroups				
	IA (n = 15)	IB (n = 15)	IIA (n = 15)	IIB (n = 15)	Norm
E, nmol/L	0.67 ± 0.02[3]	0.3 ± 0.05[3]	0.10 ± 0.40[3]	0.2 ± 0.10	0.05–0.70
FSH, mIU/mL	0.6 ± 2.2[3]	0.7 ± 2.5[3]	0.4 ± 1.8[3]	1.0 ± 0.25[3]	0.5–6.0
LH, mIU/mL	1.2 ± 0.5[3]	1.7 ± 0.9[3]	1.8 ± 0.3	0.9 ± 0. 3[3]	1.1–8.7
PG, nmol/L	0.5 ± 0.7[3]	0.01 ± 0.1[3]	0.7 ± 0.5[3]	0.02 ± 0.05[3]	0.50–6.0
PrL, mIU/L	223 ± 54.5[1.3]	687 ± 34.5[2.3]	238 ± 65.3[1.3]	669 ± 35.7[2.3]	67.0–726
C, nmol/L	564 ± 25.0[3]	674 ± 27.3[3]	655 ± 10.0[3]	670 ± 15.0[3]	150–660

[1] statistically significant differences between patients IA and IIA subgroups, p < 0,05
[2] statistically significant differences between patients IB and IIB subgroups, p < 0,05
[3] statistically significant differences between patients of the examined subgroups (comparison with table 4) before and after treatment, p < 0,05

Table 4. Levels of sex steroid hormones as a result of therapy in patients of the observation groups, follicular phase of MC

Hormone Indicators	Subgroups				
	IA (n = 15)	IB (n = 15)	IIA (n = 15)	IIB (n = 15)	Norm
E, nmol/L	0.42 ± 0.06	0.5 ± 0.15	0.12 ± 0.4	0.25 ± 0.01	0.05–0.70
FSH, mIU/mL	4.2 ± 1.2[3]	2.7 ± 2.5[3]	2.4 ± 1.8	2.6 ± 0.15[3]	0.5–6.0
LH, mIU/mL	7.2 ± 1.5[3]	3.7 ± 3.9[3]	2.2 ± 1.5	1.9 ± 0.6	1.1–8.7
PG, nmol/L	5.3 ± 0.7[3]	2.5 ± 1.5[3]	2.7 ± 0.5[3]	1.4 ± 1.5[3]	0.50–6.0
PrL, mIU/L	211 ± 42.5[1.3]	572 ± 24.0[2.3]	218 ± 34.3[1.3]	530 ± 35.7[2.3]	67.0–726
C, nmol/L	205 ± 45.0[1.3]	234 ± 27.3[2.3]	405 ± 20.0[1.3]	550 ± 12.0[2.3]	150–660

[1] statistically significant differences between patients IA and IIA subgroups, p < 0,05
[2] statistically significant differences between patients IB and IIB subgroups, p < 0,05
[3] statistically significant differences between patients of the examined subgroups (comparison with table 3) before and after treatment, p < 0,05

Table 5. Levels of sex steroid hormones before therapy in patients of observation groups, luteal phase of MC

Hormone indicators	Subgroups				
	IA (n = 15)	IB (n = 15)	IIA (n = 15)	IIB (n = 15)	Norm
E, nmol/L	0.5 ± 0.05	0.46 ± 0.02	0.8 ± 0.60	0.6 ± 0.55	0.10–1.10
FSH, mIU/mL	7.5 ± 2.3[3]	4.7 ± 2.2[3]	3.2 ± 2.2[3]	6.4 ± 1.8[3]	1.10–9.50
LH, mIU/mL	0.75 ± 0.33[3]	0.07 ± 0.03[3]	0.80 ± 0.25[3]	0.6 ± 0.3[3]	0.9–14.4
PG, nmol/L	12.0 ± 5.2[3]	10.5 ± 2.2[3]	12.4 ± 2.5[3]	8.2 ± 2.4[3]	10.0–89.0
PrL, mIU/L	223 ± 54.5[1]	637 ± 34.5[2.3]	238 ± 65.3[1]	650 ± 35.7[2.3]	67.0–726
C, nmol/L	545 ± 45.0[3]	674 ± 27.3[3]	655 ± 10.0[3]	670 ± 15.0[3]	150–660

[1] statistically significant differences between patients IA and IIA subgroups, p < 0,05
[2] statistically significant differences between patients IB and IIB subgroups, p < 0,05
[3] statistically significant differences between patients of the examined subgroups (comparison with table 6) before and after treatment, p < 0,05

Table 6. Levels of sex steroid hormones as a result of therapy in patients of observation groups, luteal phase of MC

Hormone indicators	Subgroups				
	IA (n = 15)	IB (n = 15)	IIA (n = 15)	IIB (n = 15)	Norm
E, nmol/L	0.08 ± 0.02	0.10 ± 0.02	0.12 ± 0.2	0.09 ± 0.05	0.10–1.10
FSH, mIU/mL	5.5 ± 2.4[3]	6.7 ± 2.2[2.3]	5.2 ± 2.2[3]	4.4 ± 1.8[2.3]	1.10–9.50
LH, mIU/mL	11.2 ± 2.2[1.3]	8.7 ± 2.6[2.3]	6.7 ± 2.3[1.3]	4.2 ± 1.2[2.3]	0.9–14.4
PG, nmol/L	65.2 ± 2.8[1]	58.7 ± 10.2	42.5 ± 12.3[1]	34.2 ± 10.2[2]	10.0–89.0
PrL, mIU/L	215 ± 44.8[1]	379 ± 34.0[2.3]	219 ± 34.3[1]	330 ± 35.7[2.3]	67.0–726
C, nmol/L	305 ± 35.0[3]	287 ± 27.3[3]	440 ± 15.0[3]	470 ± 10.0[3]	150–660

[1] statistically significant differences between patients IA and IIA subgroups, p < 0,05
[2] statistically significant differences between patients IB and IIB subgroups, p < 0,05
[3] statistically significant differences between patients of the examined subgroups (comparison with table 5) before and after treatment, p < 0,05

steroid hormones, FSH, LH in the studied groups did not differ significantly; there was no significant statistical difference (p> 0.05). The similarity of data in groups with a similar clinical course of menstrual disorders is noteworthy: groups IA and IIA (heavy uterine menstrual bleeding) and groups IB and IIB (scanty spotting, regular and irregular).

As a result of the 3-month therapy in patients of the main group, significantly different laboratory indicators were observed in relation to patients of the comparison group – normalized level of steroid hormones. Normalization of cortisol levels is extremely revealing in patients of subgroups treated with Tazalok™, relative to patients of comparison subgroups treated with *Vitex agnus-castus* (table 5, table 6).

Results of hormonal studies convincingly confirm complex effective action of Tazalok™ for all links of the pathogenesis of MC disorders, including ensuring a decrease in the level of PrL (which is usually was an advantage of *Vitex agnus-castus* drugs).

In addition, normalization of thyroid hormones was observed: a decrease in the level of thyroid-stimulating hormone, antibodies to thyroid peroxidase in groups of patients, taking Tazalok™. Among women taking *Vitex agnus-castus*, no such changes were found.

Extremely revealing, also, the results of ultrasound of pelvic organs, thyroid gland, breast. In patients, the main groups, the sizes of M-echo normalized (subgroup IA): before the course of treatment, the result was 14 ± 2.5 mm, at the end of 3 months of treatment with Tazalok™ it was 11 ± 1.5 mm, there was a decrease in myometrial vascularization on the eve of menstruation (increased vascularization was usually clinically associated with dysmenorrhea) (Fig. 1).

In the comparison group (subgroup IIA), the patients of which received *Vitex agnus-castus*, the sizes of the M-echo were 13 ± 3.5 mm before treatment and 12 ± 1.5 mm after; pathological vascularization of the myometrium was recorded in most cases, in 9 patients (60.0%) (Fig. 2).

In patients with follicular persistence in group IB, at the end of 3 months of Tazalok™ therapy, an echographic norm of the ovarian structure and normalization of the blood flow in the pelvis were established (Fig. 3).

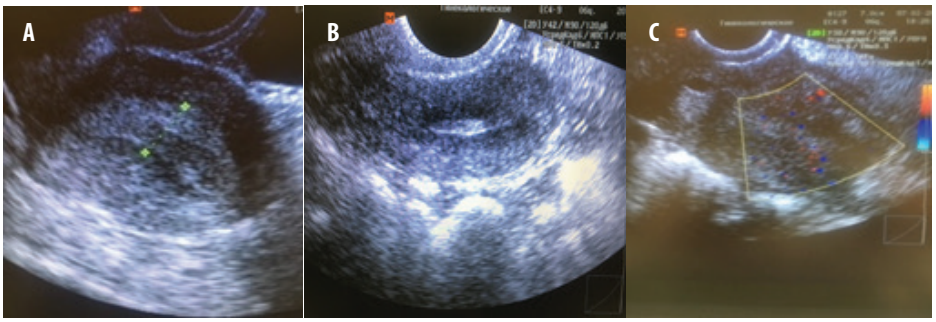

Figure 1. Patient M., group IA (Tazalok™)
A. Sonogram of the uterus on the 22nd day of MC, before the treatment - M-echo 15 mm (borderline value with hyperplasia)
B. Sonogram of the uterus on the 22nd day of the MC after therapy - M-echo 10 mm (normal)
C. Sonogram of the uterus on day 22 of the MC - normalization of blood flow in the uterus after therapy

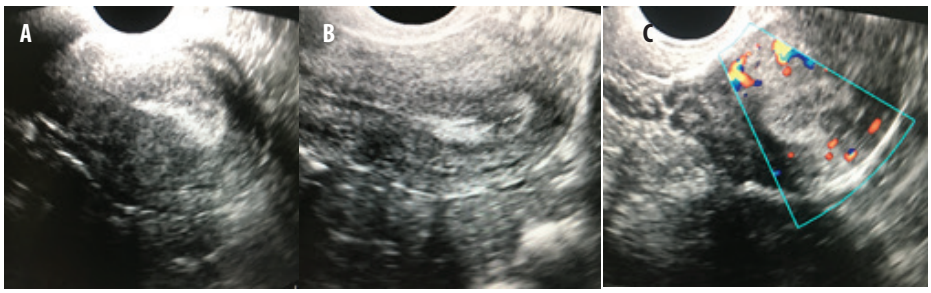

Figure 2. Patient C., group IIA (*Vitex agnus-castus*)
A. Sonogram of the uterus on day 22 of the MC, before the treatment - M-echo 14 mm
B. Sonogram of the uterus on day 22 of the MC after therapy - M-echo 11 mm
C. Sonogram of the uterus on the 22nd day of the MC after the therapy - increased vascularization of the myometrium is preserved

With thyroid ultrasound, at the end of the Tazalok™ course, normalization of the echographic density of thyroid lobes was observed (Fig. 4).

It is known that one of the earliest signs of hyperplastic changes is the rarefaction of sonographic density, the occurrence of hypoechoic sites. Sonographic control of breast tissue showed a similar pattern of normalization of echographic density, a decrease in the diameter of cystic elements, expanded milk ducts in both observation groups (Fig. 5).

Vitex agnus-castus is traditionally used in clinical cases of mastalgia. The results of this study led to the conclusion that Tazalok™ also has a regulatory effect on the condition of the breast.

Side effects were not observed in the treatment of Tazalok™, patients subjectively noted improvement in well-being already by 2-3 weeks of taking the medicine.

There was a significant reduction in pain in women who had symptoms of dysmenorrhea and mastalgia. All patients showed a significant reduction in pain, with a pain scale to low values of 1-2 points in 2 (13.3%) patients of subgroup IA and 3 (20.0%) of patients of subgroup IB, or the disappearance of symptoms.

Thus, as a result of a comparative study, we can state the advantage of the medicine Tazalok™ in the treatment of clinical manifestations of various forms of menstrual disorders compared with the *Vitex agnus-castus* drug.

CONCLUSIONS

1. Complex phytoselective preparation Tazalok™ is a highly effective medicine in the treatment of MC disorders of various clinical courses of women of reproductive age. As a result of the use of the drug, the level of steroid hormones, PrL, thyroid hormones is normalized.

2. As a result of using Tazalok™, unlike treatment with *Vitex agnus-castus*, a significant decrease in cortisol levels occurs, which expands the range of Tazalok™ use and allows reducing the number of medicines used.

3. Tazalok™ can be used as monotherapy of MC disorders with various clinical courses, and the study of the long-term effects of the medicine may be the subject of further research.

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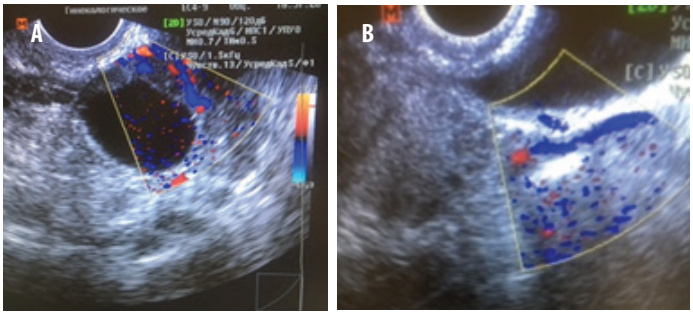

Figure 3. Patient M., group IB (Tazalok™): ultrasound normalization ovarian structures
A. Before therapy: follicle persistence, abnormal blood flow
B. After 3 months of therapy: normal ovarian structure, normalization of blood flow

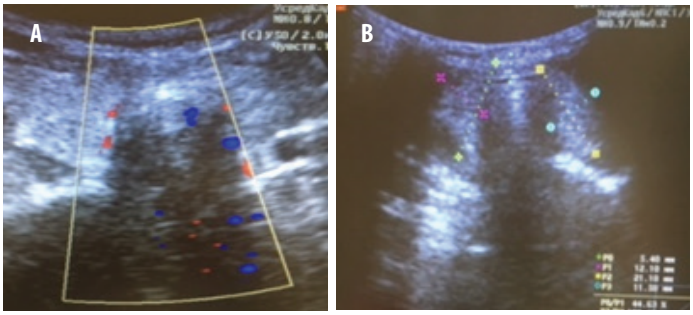

Figure 4. Patient M., group IA (Tazalok™): ultrasound normalization thyroid tissue density
A. Before therapy
B. After 3 months of therapy

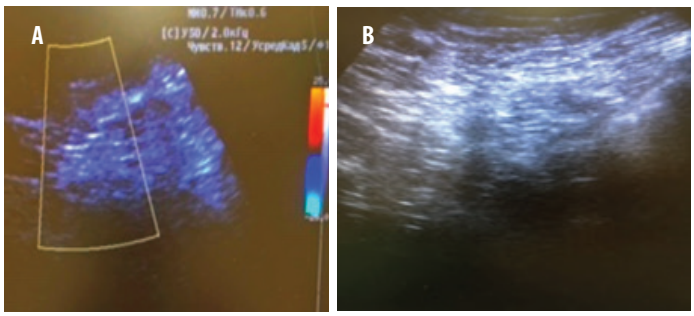

Figure 5. Patient L., group IB (Tazalok™): normalization of the echographic structure of breast tissue
A. Before therapy
B. After 3 months of therapy: a decrease in the diameter of the cystic elements of mastopathy (I phase of MC)

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NEW PATTERNS OF MENSTRUAL DISORDERS' TREATMENT – UNIFICATION OF THE METHOD

O.V. Grishchenko, MD, professor, head of the Perinatology, Obstetrics and Gynecology Department, Kharkiv Medical Academy of Postgraduate Education
V.V. Bobrytska, PhD, associate professor at the Perinatology, Obstetrics and Gynecology Department, Kharkiv Medical Academy of Postgraduate Education

Effective treatment of menstrual cycle disorders, elimination of polypragmasia, and unification of the method in various types of menstrual disorders is an important task of modern science and practice.
The aim of the study was to optimize the treatment of menstrual disorders with drugs of plant origin, by comparing the clinical efficacy of Tazalok™ and *Vitex agnus-castus*.
Design: a comparative study.
Materials and methods. Under the supervision there were 60 patients aged 23–37 years with various forms of menstrual disorders, divided into two groups of 30 people, in accordance with therapy. Patients of the main group I received Tazalok™ for treatment of menstrual disorders, 45 drops 2 times a day, patients II (comparison group) received 40 drops of *Vitex agnus-castus* 1 time per day. The course of therapy was 3 months. The main group and the comparison group were divided into two subgroups of 15 patients, in accordance with the peculiarities of the menstrual disorders. Subgroup IA of main group – patients with heavy bleeding during the menstrual period, IB – patients with scanty menstruation. In the comparison group: IIA – heavy menstrual bleeding, IIB – meager menstrual bleeding. All patients underwent a hormonal study before and after 3 months of treatment, sonographic monitoring, evaluation of subjective complaints.
Results. There was normalization of the level of steroid hormones, the thyroid gland hormones. A significant decrease in cortisol levels was in patients taking Tazalok™. Sonographic characteristics of the pelvic organs, mammary glands, and the thyroid gland in patients treated with Tazalok™ showed a positive trend, the disappearance of the pathological vascularization of target organs. Decrease in complaints by 2–3 weeks of taking.
Conclusion. Tazalok™ is an effective medicine for the treatment of various clinical forms of menstrual cycle disorders, has a wider range of effects compared with Vitex agnus-castus.

Keywords: menstrual cycle disorders, monotherapy, Tazalok.

НОВІ ПАТЕРНИ ЛІКУВАННЯ ПОРУШЕНЬ МЕНСТРУАЛЬНОГО ЦИКЛУ - УНІФІКАЦІЯ МЕТОДУ

О.В. Грищенко, д. мед. н., професор, зав. кафедрою перинатології, акушерства та гінекології ХМАПО
В.В. Бобрицька, к. мед. н., доцент кафедри перинатології, акушерства та гінекології ХМАПО

Ефективне лікування порушень менструального циклу, ліквідація поліпрагмазії, уніфікація методу при різних типах порушень менструального циклу є актуальним завданням сучасної науки і практики.
Метою дослідження була оптимізація лікування порушень менструального циклу з використанням монопрепарату рослинного походження шляхом порівняння клінічної ефективності застосування препарату Тазалок™ і препарату *Vitex agnus-castus*.
Дизайн: порівняльне дослідження.
Матеріали та методи. Під спостереженням знаходилися 60 пацієнток віком 23–37 років з різними формами порушень менструального циклу, розділені на дві групи по 30 жінок відповідно до проведеної терапії. Пацієнтки основної групи I отримували препарат Тазалок™ по 45 крапель 2 рази на день, пацієнтки II групи порівняння отримували препарат *Vitex agnus-castus* по 40 крапель 1 раз на день. Курс терапії тривав 3 місяці. Основна група і група порівняння були розділені на дві підгрупи по 15 пацієнток відповідно до особливостей порушень менструального циклу. Підгрупа IA основної групи – пацієнтки з рясними кровотечами в менструальний період, IБ – пацієнтки з мізерними менструаціями. У групі порівняння: IIA – рясні менструальні кровотечі, IIБ – мізерні менструальні кровотечі. Всім пацієнткам проводили гормональне дослідження до початку і після 3 місяців лікування, сонографічний контроль, оцінку суб'єктивних скарг.
Результати дослідження. Констатовано нормалізацію рівня стероїдних гормонів, щитовидної залози. Значне зниження рівня кортизолу спостерігалось в групах дослідження в пацієнток, які приймали Тазалок™. Сонографічна характеристика органів малого таза, молочних залоз, щитовидної залози в основній групі пацієнток, які приймали Тазалок™, демонстрували позитивну динаміку, зникнення патологічної васкуляризації органів-мішеней, зменшення скарг на 2–3-му тижні прийому препарату.
Висновок. Тазалок™ є ефективним препаратом для лікування різних клінічних форм порушень менструального циклу, має ширший спектр ефектів дії в порівнянні з *Vitex agnus-castus*.

Ключові слова: порушення менструального циклу, монотерапія, Тазалок.

НОВЫЕ ПАТТЕРНЫ ЛЕЧЕНИЯ НАРУШЕНИЙ МЕНСТРУАЛЬНОГО ЦИКЛА – УНИФИКАЦИЯ МЕТОДА

О.В. Грищенко, д. мед. н., профессор, зав. кафедрой перинатологии, акушерства и гинекологии ХМАПО
В.В. Бобрицкая, к. мед. н., доцент кафедры перинатологии, акушерства и гинекологии ХМАПО

Эффективное лечение нарушений менструального цикла, ликвидация полипрагмазии, унификация метода при различных типах нарушений менструального цикла является актуальной задачей современной науки и практики.
Целью исследования стала оптимизация лечения нарушений менструального цикла с использованием монопрепарата растительного происхождения путем сравнения клинической эффективности применения препарата Тазалок™ и препарата *Vitex agnus-castus*.
Дизайн: сравнительное исследование.
Материалы и методы. Под наблюдением находились 60 пациенток в возрасте 23–37 лет с различными формами нарушений менструального цикла, разделенные на две группы по 30 женщин в соответствии с проводимой терапией. Пациентки основной группы I получали препарат Тазалок™ по 45 капель 2 раза в день, пациентки II группы сравнения получали препарат *Vitex agnus-castus* по 40 капель 1 раз в день. Курс терапии составил 3 месяца. Основная группа и группа сравнения были разделены на две подгруппы по 15 пациенток в соответствии с особенностями нарушений менструального цикла. Подгруппа IA основной группы – пациентки с обильными кровотечениями в менструальный период, IБ – пациентки со скудными менструациями. В группе сравнения: IIA – обильные менструальные кровотечения, IIБ – скудные менструальные кровотечения. Всем пациенткам проводили гормональное исследование до начала и после 3 месяцев лечения, сонографический контроль, оценку субъективных жалоб.
Результаты исследования. Констатирована нормализация уровня стероидных гормонов, щитовидной железы. Значительное снижение уровня кортизола наблюдалось в группах исследования у пациенток, принимавших Тазалок™. Сонографическая характеристика органов малого таза, молочных желез, щитовидной железы в основной группе у пациенток, принимавших Тазалок™, демонстрировали положительную динамику, исчезновение патологической васкуляризации органов-мишеней, уменьшение жалоб к 2–3 неделе приема прапарата.
Вывод. Тазалок™ является эффективным препаратом для лечения различных клинических форм нарушений менструального цикла, имеет более широкий спектр действия по сравнению с *Vitex agnus-castus*.

Ключевые слова: нарушение менструального цикла, монотерапия, Тазалок.