



PREMENSTRUAL SYNDROME IN THE MODERN SCIENCE

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Introduction. The results of a number of studies suggest that emotionally labile patients with ethnic physique, underweight, as well as women engaged in intellectual work are susceptible to PMS [6, 7] Among the risk factors for PMS are heredity, acute or chronic emotional stress, previous gynecological diseases, mental illness, mental and emotional stress, etc. [3, 5]. There are several theories that represent the etiopathogenetic mechanisms of PMS: hormonal, allergic, the theory of "water intoxication", hyper adrenocortical activity and an increase in aldosterone, psychosomatic theory. However, regardless of the theoretical justification in PMS, secretion is always impaired main hormones: estrogens, progesterone, serotonin, regulating the luteal phase of the menstrual cycle [2, 3].

Premenstrual syndrome (PMS), or premenstrual tension syndrome, is considered not as a disease, but as a complex symptom complex is a pathological condition characterized by cyclically repeating physical, psycho-emotional, behavioral symptoms that develop in the luteal phase of the cycle (2-14 days before menstruation) and disappear as that comes. Some researchers believe that PMS occurs in every woman, but manifests itself as mild symptoms that are not regarded by a woman as a painful condition [1-3].

The prevalence of PMS varies from 30 to 95%, including from 2 to 19% of women suffer from several forms. The incidence of PMS increases with age: from 19 to 29 years old, this condition is observed in 20%, after 30 - in 47%, after 40 - in 55% of women [4, 5].

Although the exact cause of PMS is not fully established, there is some evidence that premenstrual symptoms may be accompanied by latent hyperprolactinemia (LHP) [8, 9], an increase in prolactin occurs either before menstruation or in response to stressful situations [10, 11]. Elevated prolactin level can inhibit, the development of lutein in the body, thereby indirectly reducing the secretion of progesterone in the luteal phase of the menstrual cycle [12]. LHP has been associated with premenstrual mastalgia, benign changes in the mammary glands (fibrocystic disease) and infertility [13, 14]

Depending on the prevalence of certain manifestations in the clinical picture, four forms of PMS: neuropsychic, edematous, cephalic, crisis. All the many PMS symptoms can be divided into behavioral and physical Behavioral include fatigue, irritability, forgetfulness, sleep disturbance, labile mood, intense anger, conflicts with other people, decreased interest in ordinary activities, social isolation, difficulty concentrating. Physical-impaired appetite, various gastrointestinal disorders, up to nausea and vomiting, breast tenderness - mastalgia, muscle and headaches, fever, swelling, weight gain, etc. The abundance of manifestations - more than 200 symptoms are known today - are due to the complex etiology of PMS [15, 16].

There are no reliable and publicly available criteria for diagnosing PMS. It is necessary to rely, first of all, on a carefully collected anamnesis and characteristic clinical symptoms (psycho-emotional, metabolic endocrine, etc.), the cyclical nature of their manifestation (before

menstruation) and its appearance (after it). PMS is diagnosed in accordance with ICD-10 criteria (N94.3 Premenstrual tension syndrome), in the presence of one or more symptoms and frequency (symptoms bother a woman only in the luteal phase of the menstrual cycle).

Differential diagnosis of PMS is primarily carried out with various mental illnesses, since neuropsychiatric symptoms often prevail in its clinical picture. It is required to exclude major depression, dysthymic states, generalized anxiety, panic disorders, bipolar disorders. Anemia, autoimmune diseases, hypothyroidism, diabetes, convulsions, endometriosis, chronic fatigue syndrome, etc. can have similar symptoms [17, 18]

Before prescribing treatment, a comprehensive examination is required to identify gynecological and concomitant extragenital pathology. If necessary, consultations should involve related specialists: neuropsychiatrist, gastroenterologist, therapist. A deeper examination, possible to perform a molecular genetic study.

Of course, PMS is a multifaceted pathological condition that affects a woman's quality of life. Quality of life is an indicator that integrates the physical, psychological, emotional and social characteristics of a person, which, in general, reflects his ability to adapt to the manifestations of the disease. Women with PMS have the ability to adapt to the manifestations of the disease and social activities (at work, in life) are significantly violated. They are characterized by frequent unjustified mood swings, aggressiveness and increased conflict, depressive states, sometimes quite difficult. All this significantly reduces the quality of life of a woman as a whole

PMS treatment. PMS treatment should be individualized, taking into account the patient's complaints and symptoms. Among the main principles and methods of PMS treatment adhering to work and rest, regular sports, and balanced nutrition.

Herbal medicine plays an important role in the treatment of PMS - the use of herbal medicines. Since herbal medicines are medicines created from plant extracts, which, in turn, from plant cells, they have much in common in structure with substances formed in the cells of animals and humans. The tolerance of these substances is much better than those with a chemical basis. In addition, side reactions when taking herbal drugs are less common, often they are not so significant and less pronounced. Herbal drugs have significantly fewer contraindications. The effect of herbal drugs occurs more slowly, but it is more persistent and lasting than that of synthetic drugs. Herbal medicine is traditionally used to treat many diseases [7-9, 19-22]

Sacred Vitex-castus is a plant characteristic of the Mediterranean region. The main chemical composition of this plant contains vitexin, castic in, agnuside, phydroxy benzoic acid, alkaloids, diterpenoids. Its fruits contain flavonoids, terpenoids, neolignans, phenolic compounds, etc. The plant has a positive effect on many pathological conditions, including PMS, mastalgia, inflammation and sexual dysfunction, and also helps relieve pain by having an antinociceptive (analgesic) effect [23 -25]. Sacred Vitex-castus is effective in reducing the symptoms of many gynecological problems. It is clinically used for abnormal uterine bleeding, mastodynia, PMS. Herbal drugs based on Sacred Vitex-castus are used for mild hyperprolactinemia, luteal phase defect, menorrhagia, they reduce discomfort and pain during menstruation, can be prescribed for women with uterine fibroids, polycystic ovary syndrome. Sacred Vitex is known all over the world and has been used since ancient times. It has dopaminergic properties, influencing the pathogenetic mechanisms of PMS development: secretion of prolactin, gonadotropic releasing hormone, follicle-stimulating and luteinizing hormones. Due to

these effects, the drug selectively block skicks synthesis prolactin, reduces level follicle-stimulating elimination of the imbalance of sex hormones, exhibits an antioxidant effect, acts on opioid receptors.

Clinical research evidence suggests that herbal medicine provides a prerequisite for the treatment of certain diseases. Organic, cost-effective hormone, promotes phytopreparations that are highly effective, compatible with the body and have a minimum of side effects are an alternative in the treatment of certain diseases. A number of studies have been carried out to study plants with useful chemical and pharmacological structures. The National Association for Premenstrual Syndrome (UK) presented an updated guideline in 2016, high lighting the efficacy of a phyto-drug based on the fruit of Sacred Vitex - castus (recommendation grade B). In 2016, the Royal College of Obstetricians and Gynecologists of Great Britain presented guidelines for the management of women with PMS, which recommends the use, in addition to vitamin preparations, of herbal extracts -ginkgo biloba, saffron and sacred vitex [26].

Two drugs containing sacred vitex are successfully used all over the world – Mastodinone and Cyclodinone.

Cyclodinone is a herbal monopreparation. It is prescribed for the treatment of menstrual irregular ities caused by insufficient luteal phase. The drug also affects PMS symptoms, eliminating headache, edema, normalizing mental lability, mastalgia. The course of treatment is at least three months, without interruptions for the period of menstruation, and, if necessary, can be extended. Statistically significant changes were obtained treatment cycles compared with the initial data. At the same time, no patient experienced adverse reactions while taking a drug containing sacred vitex [27]. Kulakov's study confirmed the effectiveness of the use of Cyclodinone in women with moderate and severe PMS.A significant decrease in the manifestations of PMS and an improvement in the quality of life were noted [3].

Another study examined the quality of life of patients with moderate and severe PMS before and after treatment with a phytopreparation based on Vitexbounded and combined OC containing 20 mg ethinylestradiol and 3 mg drospirenone in a 24 + 4regimen. The condition of the patients, their quality of life improved. A more pronounced effect was noted inrelation to metabolic-endocrine and physical manifestations of PMS (decreased appetite, bloating, mastodinia, mastalgia and pain manifestations) [6]. Of interest are studies comparing the results of using Vitex extract and fluoxetine in the treatment of PMDD (premenstrual dysphoric disorder). Clinical improvement was observed within 8 weeks in 57.9% of20 participants who received Vitex extract (20 –40 mg /day), compared with 68.4% of 21 participants receiving fluoxetine (20-40 mg / day). Symptoms such as irritation breasts, swelling, excessive appetite, depression, irritability, insomnia, nervous tension, feeling out of control, lower abdominal pain. It was concluded that fluoxetine may be more effective for psychological symptoms, while sacred vitex may be more effective for physical symptoms [28].

Mastodinon is a combined drug The drug has beenshown to be most effective in the treatment of fibrocysticmastopathy, mastodynia syndrome, and PMS. The duration of the course of treatment is at least three months without interruption during menstruation.

In a number of studies, it has been proven that Mastodinon normalizes the state of the autonomic nervous system in PMS and relieves painful conditions in the mammary glands. A study conducted in 2011showed a positive dynamics of the Kerdo index, which reflects the presence and degree of autonomic imbalance between the sympathetic and a parasympathetic effect on the cardiovascular system during treatment with Mastodinon. Patients after therapy with

Mastodinon showed normalization of the functional state of the sympathetic and parasympathetic parts of the autonomic nervous system. It has been proven that the dopaminergic effect of Mastodinon® affects the level of prolactin. It is the Sacred Vitex -castus extract that contains dopaminergic compounds belonging to diterpenes, and by binding to dopamine-2 (DA-2) receptors, it exhibits dopaminergic activity, which subsequently leads to inhibition of prolactin and normalization of the ratio of hormones at the level of target organs, which, in turn, reduces the risk of benign changes in the mammary glands [13]. Studies demonstrate the efficacy of Mastodinon in the treatment of mastalgia. More than 70% of patients who took Mastodinon for three months experienced a decrease in mastalgia intensity. A systematic review of the healing effects of sacred Vitex extract showed that the safety profile was excellent overall for Vitex extracts in all trials, with adverse events being mild and usually infrequent. The quality of the trials ranged from weak to very good, with the majority being assessed as good, and the reliability of the studies was high [17, 18, 29, 30]. The range of tools used is quite wide. Hormones, antidepressants, diuretics, various vitamins and microelements are prescribed, the benefits of which have been confirmed by a number of studies, antispasmodics, non-steroidal anti-inflammatory drugs, in case of an allergic reaction - antihistamines, vascular drugs to improve blood circulation in the central nervous system, it is recommended to change the diet and exercise regularly, if necessary, psychotherapy is carried out. Micronized combined oral contraceptives (OC), gestagenic drugs are used as hormonal therapy [30].

A large number of publications talk about the successful use of vitamins and microelements in PMS.

Pyridoxine (vitamin B6) [31] is a cofactor necessary for the synthesis of catecholamines and dopamine. Vitamin corrects metabolism in neurotransmitters, which justifies its use in depression, irritability, edema, headache, meteorism. Vitamin E relieves mastalgia and can be prescribed during the entire menstrual cycle, but better - in the luteal phase. Magnesium deficiency can lead to PMS symptoms, and women who received magnesium-containing supplements reported improvement. Calcium deficiency may play a role in the formation of PMS symptoms. For example, while taking calcium 500mg 2 times a day for three months in women with PMS, the level of fatigue and the severity of depression significantly decreased, which was confirmed in a placebo-controlled study [28].

For the correction of mental disorders in PMS, it is proposed to use selective serotonin reuptake inhibitors as the first line: fluoxetine, sertraline, paroxetine, citalopram including headache, nausea, insomnia, fatigue, diarrhea, dizziness, decreased libido, decreased concentration [32]. But in severe mental disorders, including depression, a woman should be consulted by a psychiatrist or neuropsychiatrist [29, 30].

Oral contraceptives are an effective treatment for PMS. They suppress ovulation, reduce the thickness of the endometrium, which, in turn, leads to a decrease in the volume of menstrual blood loss, reduces the level of prostaglandin and, accordingly, reduces pain associated with uterine contraction [27, 33]. Some of the side effects of OCs, such as nausea, fluid retention, weightgain, may be a reason to stop taking PMS medications. Still, OCs are one of the drugs of choice for PMS today. Basically, these are drospirenone-containing drugs that have a number of positive properties [30]. It is preferable to prescribe hormonal contraceptives in a prolonged mode. Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen reduce the activity of the myometrium by inhibiting prostaglandin synthesis and decreasing the se-

cretion of vasopressin include bleeding, exacerbation of peptic ulcer disease, vomiting and diarrhea.

Conclusion. PMS is a pathological complex of symptoms that significantly reduces the quality of a woman's life. Its etiology and pathogenesis have not been sufficiently studied so far, but the directions in diagnosis, treatment and prevention have been identified, which must be followed. PMS treatment should be differentiated – those that take into account the state of general and reproductive health of a woman, comorbidities, severity of PMS, etc. Treatment must be carried out for every patient in order to prevent the transition of a mild form of PMS to a severe one. An important role is played by preventivemeasures aimed at improving the physical and psychoemotional state of a woman with the help of diet, maximum reduction of psycho-emotional stress, image correction life, exercise and possibly physical therapy. Herbal drugs, which are based on Vitex agnus castus, are successfully used for PMS, improving the quality of life of a woman. Studies have noted a number of advantages of phytopreparations over synthetic agents: a wide therapeutic spectrum of action, a favorable safety profile, good tolerance, practically no side effects In addition, phytopreparations can be used for as long as necessary. And, importantly, phytopreparations can be used by women who have contraindications to hormone therapy.

Today, preparations based on sacred vitex extract a reavailable in various pharmaceutical forms, including tinctures, liquid extracts, tablets and homeopathic medicines, and are widely used throughout the rest of the world

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