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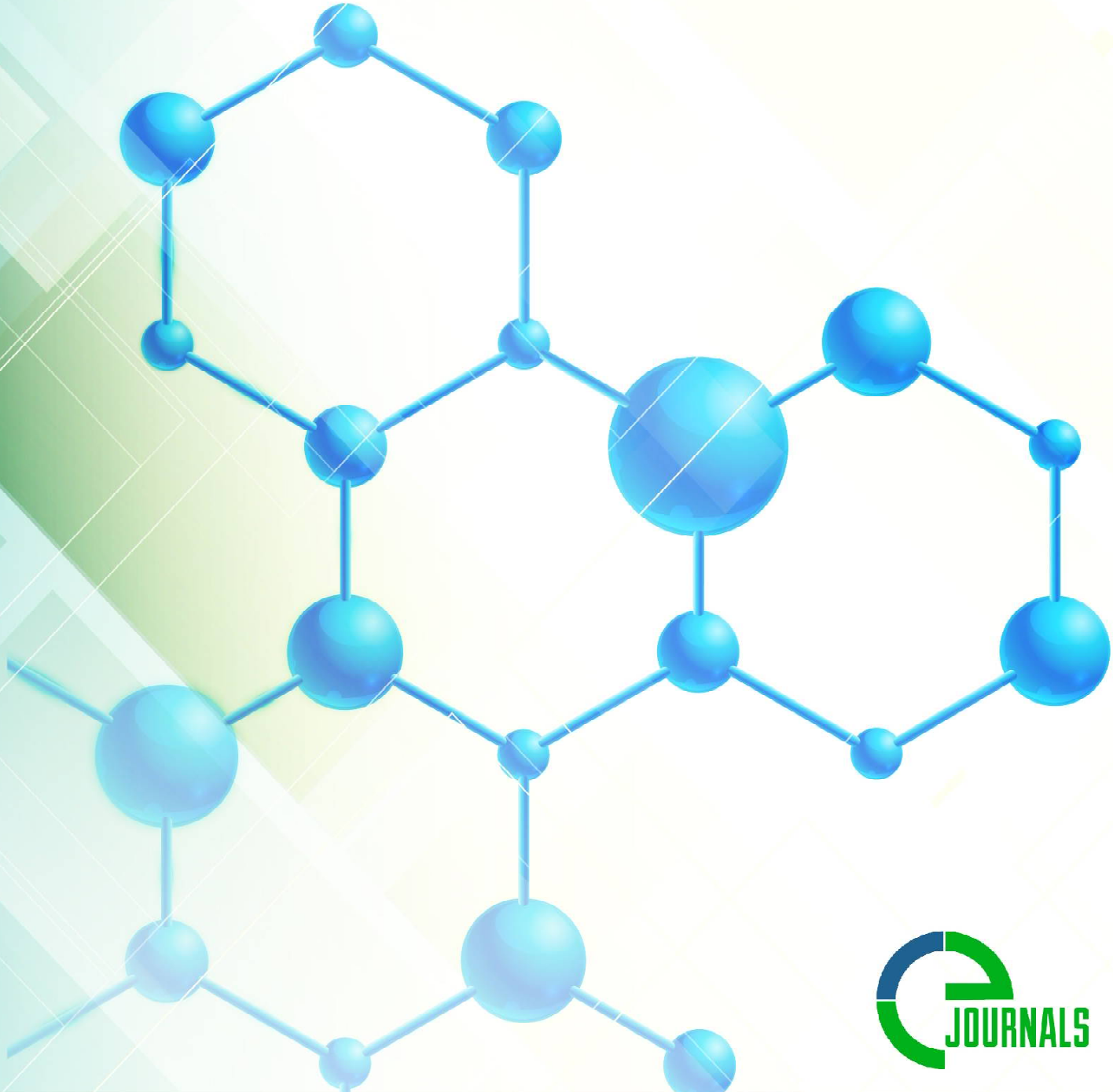

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PHARMACOLOGICAL TREATMENT OF FIBROUS CYSTIC MASTOPATHY WITH THYROID DISORDERS

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Key words: fibrous cystic mastopathy, natural compounds, anti-inflammatory activity.

Relevance of the problem.

Benign breast disease (mastopathy) - is a complex of processes characterized by a wide range of proliferative and regressive changes in the tissues of the mammary glands with the formation of abnormal ratios of epithelial and connective tissue components and the formation in the mammary gland of changes of a fibrous, cystic, proliferative nature, which often, but not necessarily, coexist (WHO definition, 1984) .

Benign breast disease (mastopathy) in women is a very common finding and results in a diagnosis in approximately one million women annually in the United States [35].

Benign Breast Disease (BBD) is one of the most important risk factors for breast cancer. Breast cancer is more common in women with BBD than in the general population [35].

The basis for the various rearrangements of the mammary glands are changes in the endocrine system, in connection with which diseases are called dyshormonal rearrangements, dyshormonal hyperplasias, dyshormonal processes.

The results of a retrospective analysis of the incidence of patients with breast cancer (BC) indicate a 2.5-4 times higher incidence of different forms of mastopathy compared with a group of women without cancer. [14].

There is no single point of view on the treatment of mastopathy. On the one hand, there is a problem of overdiagnosis of mastopathy and polypharmacy, when doctors prescribe a variety of medications and non-pharmacological agents to the patient. On the other hand, there is a clear underestimation of the problem of mastopathy, when doctors believe that since mastopathy is present in more than 1/2 of the female population, there is no need to treat this pathology.

Mastopathy is one of the most common diseases in women in any society. Up to 30% of women suffer from mastopathy at any time of their lives, and this makes them accept treatment [25].

Mastopathy is a biomarker of hormonal (at the level of the body) and tissue (at the level of the mammary glands) trouble.Multi ple etiological factors disrupt the hormonal balance in the woman's body, cause hyperestrogenism and hyperproliferation of the epithelium in the mammary gland tissue, which underlies the pathogenesis of mastopathy. Etiological factors of mastopathy and breast cancer risk factors for the most part coincide. The pathogenesis of proliferative forms of mastopathy and breast cancer has a lot in common [3].

In clinical practice, the most convenient classification takes into account clinical, morphological and radiological or ultrasound manifestations of changes in the mammary glands [27]:

1. Diffuse fibrocystic breast disease (FCD):

-diffuse mastopathy with a predominance of the cystic component;

-diffuse mastopathy with a predominance of the fibrous component;

- diffuse mastopathy with a predominance of the glandular component;
- mixed form of diffuse mastopathy;
- sclerosing adenosis.

2. Nodal form FCD .

In addition, proliferative and non-proliferative forms of mastopathy are distinguished.

Due to the polyetiological nature of this pathology, there is currently no single generally accepted standard in the treatment of mastopathy.

The algorithm for the treatment of mastopathy consists of 3 stages;

Stage I - elimination of etiological factors;

Stage II - pathogenetic therapy, normalization of neuroendocrine disorders;

Stage III - rehabilitation - long-term support of the functioning of the mammary glands at the physiological level.

The main principle of the treatment of breast pathology is the impact on the root cause of the disease. Therefore, treatment by a gynecologist must be carried out for patients with pathology of the reproductive system; at the endocrinologist - for patients with endocrine pathology; from a therapist - if there is an organic pathology of the digestive tract and liver; from a psychotherapist or neuropathologist - with mastopathy of central genesis [15].

Pathogenetic treatment of mastopathy is aimed not only at improving the quality of life, but also at preventing breast cancer [3].

Drug-free treatment:

The principles of ahealthy lifestyle include [9, 17]:

- Rational nutrition, implying limiting the calorie content of foods, the predominant consumption of vegetable fats, saturation of the diet with seafood, vegetables, fruits leads to a decrease in the incidence of diseases of the mammary glands. A factor in the prevention of breast diseases is the enrichment of the diet with foods containing selenium, manganese, zinc, iodine, vitamins A, E, C, D, group B (folates, B1, B2, B5 and especially B6), linolenic acid, etc. [17].

- Many experiments and clinical studies have shown that there is aclose relationship between the use of methylxanthines (caffeine, theophylline, theobromine) and the development of fibrocystic breast disease. It is believed that these compounds contribute to the development of fibrous tissue and the formation of fluid in cysts. That is why limiting or avoiding foods containing methylxanthines (coffee, tea, chocolate, cocoa, cola) can significantly reduce pain and swelling of the mammary glands.. [16].

- Both mastopathy and breast cancer are associated with sluggish bowel activity, chronic constipation, altered intestinal microfloraand insufficient fiber in the daily diet. Perhaps, in this case, estrogens already excreted in the bile are reabsorbed from the intestine. In this regard, patients are shown to consume food rich in fiber and adequate fluid intake (at least 1.5-2 liters per day). Since estrogen is utilized in the liver, any dietary disturbances that impede or limit normal liver function (cholestasis, fat-rich foods, alcohol, other hepatotoxic substances) over time can affect estrogen clearance in the body. [16].

- Non-drug approaches to correcting mastalgia include psychotherapy and the use of properly fitted underwear, with only 15% requiring treatment. (Strength of recommendation B) [6]. Often, when these causes are eliminated, pain in the mammary gland decreases or even completely disappears. [16].

Medication, conservative treatment;

Medication, conservative treatment includes an individual doctor's approach. Many non-hormonal and hormonal drugs, variants, schemes and methods of their application have been proposed. The short duration of the effect or failure of the applied therapy is

often associated only with symptomatic treatment and the lack of an individual analysis of genetic factors, hormonal status, the presence of concomitant gynecological, somatic and endocrine pathologies, peculiarities of the psychoemotional background and sexual life of women [15].

The goal of conservative treatment in FCD is to improve the quality of life by eliminating the subjective manifestations of the disease and stopping the morphological progression of the process [13].

Systemic drugs

1. Non-hormonal drugs

A. Phytopreparations. One of the modern non-hormonal drugs available on the domestic market is Mamoklam [13].

The drug is made from the lipid complexof brown seaweed kelp.The mechanisms of the therapeutic action of Mamoklam in patients with FCD are associated with the content of iodine, polyunsaturated fatty acids (PUFA) of the omega-3 type and chlorophyll in this agent. The composition of Mamoklam is represented by the following components: iodine in organic form - 100 ?g, omega-3 PUFA - 40 mg, chlorophyll - 10 mg [15]. Iodine in the mammary gland tissues binds to lipids, which regulate the processes of breast cell proliferation and have an antioxidant effect [15]. Therefore, chronic iodine deficiency in the diet contributes to the development of mastopathy. According to epidemiological, clinical and experimental studies, iodine reduces the risk of breast cancer [3]. Omega-3 PUFAs normalize the balance of sex hormones by interfering with the synthesis of prostaglandins, which may explain their therapeutic effect in PCB. Chlorophyll has antioxidant, anti-inflammatory, anti-mutagenic and anti-carcinogenic effects [15].

In accordance with the instructions, the drug Mamoklam should be taken orally before meals, a single dose is 1-2 tablets, 2-3 times a day at regular intervals during the day (daily dose of 3-6 tablets). The duration of the course of treatment ranges from 1 to 3 months. If necessary, it is recommended to repeat courses of treatment after a break from 2 weeks to 3 months. [13]. Pathogenetic treatment of mastopathy with the drug Mamoklam has a therapeutic effect in patients with mastopathy and, with prolonged use, reduces the risk of breast cancer [3].

Among non-hormonal drugs, a special place is occupied by phytopreparations based on the extract of the fruits of the sacred vitex (Vitex agnus - castus), which mastodinon has long been used to treat gynecological diseases.

There is convincing evidence of the effectiveness of the use of drugs based on Vitex sacred and drugs of progesterone in mastopathy (Level of persuasion of recommendations A (level of evidence - 1a) [10].

Vitex agnus-castus (VAC) preparations contain active substances - bicyclic terpenes, which have a stimulating effect on the dopamine D2 receptors of the anterior pituitary gland, which leads to a decrease in the production of adenosine monophosphate (AMP) and an increase in the production of dopamine, which inhibits the secretion of prolactin, including with "stress" and latent hyperprolactinemia, transient secretion disorders. Against the background of the normalization of prolactin secretion, the full-fledged luteal phase is restored, the phenomena of relative estrogen dominance are eliminated [2], there is a regression of pathological processes in the mammary glands, relief of mastalgia in mastopathy and premenstrual syndrome [30, 33].

A number of components of the sacred vitex extract (vitexin, casticin, isoorientin, kaempferol) exhibit antianginal and sedative effects. In 2017, two systematic reviews of clinical trials were published confirming the efficacy and safety of Vitex sacred extract in correcting latent hyperprolactinemia associated with luteal phase failure and symptoms

of cyclic mastalgia, PMS and premenstrual dysphoric syndrome (PMDS). [23, 32].

A number of scientific works prove the effectiveness of the use of mastodinone in the treatment of diffuse fibrocystic disease. In the course of our study, the high efficacy of this drug in the relief of mastalgia, assessed by the VAS scale (Visual analogue scale), in patients with various forms of diffuse mastopathy during the menopausal transition was shown, noted against the background of normalization of prolactin levels [7, 11].

Other herbal homeopathic components in combination with Agnus castus will be no less useful: Caulophyllum thalictroides D4 (basilicus stemleaf) - used for menstrual disorders; Cyclamen D4 (European cyclamen) - is prescribed for headaches, nervous and mental disorders, as well as for menstrual irregularities; Ignatia D6 (bitter chestnut) - effective for nervous disorders, prescribed for the treatment of migraine; Lilium tigrinum D3 (tiger lily) - used for symptoms of dysmenorrhea and increased irritability [12,16].

Recently, non-hormonal phytopreparations have appeared that effectively normalize hormonal status. One of these drugs is Indinol, derived from cruciferous plants. It regulates the metabolism of estrogens, suppressing the aggressive 16 - ? hydroxyestrone, inhibits the formation of estrogen receptors, neutralizes the action of tumor growth factors, has apowerful antiproliferative effect, and induces apoptosis in tumor cells of epithelial origin. The drug is effective in cystic forms and diffuse-nodular variants of FCM, especially in pathology of the genital area. It is prescribed 2 capsules 2 times a day for 3-6 months [12].

A. Non-steroidal anti-inflammatory drugs (NSAIDs)

Effective means for correcting mastalgia are non-steroidal anti-inflammatory drugs (NSAIDs) for both systemic and local use (Strength of recommendations A (level of evidence - 1b) Antiprostaglandins - nimesulide, indomethacin, ibuprofen, diclofenac - reduce the production of prostaglandins and are used to relieve premenstrual edema and soreness of the mammary glands [10].

B. Thyroid drugs. Due to the fact that mastopathy is often associated with diseases of the thyroid gland, including autoimmune thyroiditis, the use of potassium iodide without appropriate examination is not recommended [19]. With hypofunction of the thyroid gland, especially with a combination of hyperprolactinemia with an increased TSH content, Levothyroxine sodium is shown at a dose of 25-50 ?g per day for 3-6 months under the control of TSH levels [10].

G. Biguanides. One of the possible promising areas of pathogenetic effects on breast tissue in FCD associated with insulin resistance and not only is the use of biguanides, in particular metformin. For the first time J. Evans et al. noted that the use of metformin in patients with diabetes mellitus can be combined with a decrease in the risk of developing malignant neoplasms. The main intracellular target for the antitumor effect of metformin is considered adenosine - onophosphate kinase (AMPK), the activation of which inhibits the mTOr- (mammalian target of rapamycin) signaling pathway, as a result of which the synthesis of a number of proteins is inhibited, the level of cyclin D1 decreases, and the cell cycle block is initiated [26] .

Clinical trials on the use of metformin in breast cancer are ongoing. Experience is gradually accumulating in the use of metformin in women without carbohydrate metabolism disorders [24] in the protocols of neoadjuvant therapy for breast cancer (METTEN study, 2010).

Hormonal drugs

Hormone therapy most effectively affects the epithelial component of FCD [10].

A. Antiestrogens. For the treatment of mastopathy, antiestrogens, tamoxifen, are used, the mechanism of action of which is based on competitive binding with estradiol

receptors in breast tissue cells. The recommended dose is 10-20 mg per day for a course lasting from 3 to 6 months. It was found that after 2 weeks of taking the drug, there was a decrease in the level of gonadotropins and, accordingly, suppression of ovarian function. After 10-12 weeks. taking the drug decreases the symptoms of mastalgia, radiographically, there is a decrease in the areas of compaction in the gland. Contraindications to its use: thrombophlebitis, pregnancy, disorders of the blood coagulation system. Fareston (Toremifen) has fewer side effects, it is prescribed at 10 - 20 - 30 mg per day for 1 - 3 months continuously. After a month, the course of treatment can be repeated. Among the drugs for the correction of mastalgia, tamoxifen is also effective (at a dose of 10 mg daily for 3-6 months, and if it is ineffective, danazol at a dose of 200 mg daily or only in the luteal phase of the menstrual cycle (level of persuasion of recommendations A (level of evidence) - 1a), although their use is limited due to side effects.In addition, in the Russian Federation, DMZ is not an official indication for the use of tamoxifen [10].

One of the modern synthetic drugs is Livial. Livial (tibolone) has estrogenic, gestagenic and weak androgenic properties, reduces the rate of proliferation of breast cells, has an antiestrogenic effect on the epithelial component, promoting apoptosis. At a dose of 2.5 mg, it suppresses the secretion of gonadotropins, without stimulating the proliferation of the endometrium, and inhibits ovulation. Apply at 2.5 mg / day for 1-3 months. Contraindications to the use of the drug: pregnancy, hormone-dependent tumors, thrombosis, bleeding from the genital tract of unknown etiology [5].

B. Progesterones. The classical dosage forms are Primolut-nor, used at 5 mg / day from the 16th to the 25th day of the menstrual cycle; Duphaston is an analogue of natural progesterone without androgenic, estrogenic and corticosteroid activity, it is prescribed at 5-10 mg in the second phase of the cycle; Utrojestan is a natural micronized progesterone for oral or intravaginal use without androgen-like and anabolic effects. Due to the identity of the drug and endogenous progesterone, it has a good efficacy and safety profile. Moreover, if the patient has hepatopathy, Utrojestan can be used intravaginally, which eliminates the negative systemic effect. The drug is prescribed 100 mg 2-3 times a day from the 17th day of the menstrual cycle for 10-14 days (the course of treatment is 3-6 cycles). Utrojestan is especially indicated for patients with FCD in combination with adenomyosis, endometrial hyperplasia and uterine myoma [4].

B. Inhibitors of the pituitary gonadotropic function. Agonists of the gonadotropin-releasing hormone of the pituitary gland - Goserelin, Buserelin and others, competitively interacting with the receptors of the cells of the anterior lobe of the pituitary gland, lead to a blockade of the gonadotropic function of the pituitary gland, preventing the production of LH and FSH. The drugs are prescribed when mastopathy is combined with severe endometriosis, accompanied by severe pain syndrome and / or menometrorrhagia. The course of treatment is 3-6 months. The result is reversible menopause. To minimize the manifestations of estrogen deficiency, low doses of HRT are simultaneously prescribed.

Diphereline (asynthetic analogue of gonadotropin-releasing hormone of the pituitary gland) leads to a decrease in the level of ovarian hormones to the castration level within 2 weeks from the start of treatment.Diphereline is administered intramuscularly at adose of 3.75 mg once every 28 days or 11.25 mg once every 90 days.

Danazol (Danol, Danoval) has a weak androgen-like effect with anabolic effect, suppresses the production of LH and FSH by the pituitary gland and blocks the enzymes of steroidogenesis in the ovaries and adrenal glands. The drug is prescribed in a dose of 50-100 mg per day for 1-2 months. Nemestran (gestrinone) is a 3rd generation norsteroid with antigonadotropic, antiestrogenic and antiprogesterone effects.Prescribe the drug 2.5 mg once a week for 6 months [10].

Side effects of danazol include amenorrhea, weight gain, changes in blood pressure, acne, etc. Contraindications to the use of the drug are pregnancy, lactation, porphyria [31]. The effectiveness of the correction of mastalgia with the use of agonists of gonadotropin-releasing hormone of the pituitary gland has been proven, however, the duration of use of these drugs is limited due to manifestations of estrogen deficiency and in women with mastopathy, they are usually prescribed for other indications. (Strength of recommendation A (level of evidence - 1a) [10].

G. Dopamine agonists. Dopamine agonists are predominantly used in hyperprolactinemia (ICD code E 22.1), in accordance with the clinical guidelines of the Russian Association of Endocrinologists [9], however, prolactin inhibitors can also be effectively used in the treatment of mastopathy [22], (Strength of recommendation A (level of evidence - 1b).

Dopamine agonists - stimulate dopamine receptors, mainly of the D2 type, thereby inhibiting the production of prolactin, reduce the activity of estrogen receptors and thus have an indirect antiestrogenic effect. The following dopamine agonists are currently registered [9, 28]:

Quinagolide is a non-ergoline selective dopamine receptor agonist. The initial dose is 25 mcg per day, with a gradual increase every 3-5 days by 25 mcg. The average daily dose is about 75 mcg, maximum 300 mcg.

Bromocriptine is an ergoline dopamine receptor agonist.Bromocriptine drugs were the first to be used to treat hyperprolactinemia more than 30 years ago. Unlike cabergoline, bromocriptine is anon-selective agonist of dopamine receptors in the brain, which leads to more side effects. The initial dosage is 0.62-1.25 mg per day, the therapeutic range is 2.5-7.5 mg per day.

Cabergoline is an ergoline selective dopamine D2 receptor agonist. The long half-life allows the drug to be used 1-2 times a week. The initial dosage is 0.25-0.5 mg per week, followed by increasing the dose until the prolactin level normalizes. As a rule, the average dose is 1 mg / week, although in cases of resistant prolactinomas it can be 3-4.5 mg for a week.

Cabergoline is the first-line drug as the most effective in normalizing prolactin levels and reducing tumor size. (Evidence level 1, recommendation grade A)

Side effects of dopamine agonist therapy:

- from the gastrointestinal tract: decreased appetite, nausea, vomiting, constipation, dyspepsia.
- from the nervous system: dizziness, headache, drowsiness, weakness, insomnia.
- on the part of the cardiovascular system: postural hypotension, orthostatic collapse.

D. Combined oral contraceptives. Combined oral contraceptives have been used with success since the middle of the last century. The mechanism of their action is associated with the suppression of the gonadotropic function of the pituitary gland through the suppression of the secretory activity of the hypothalamus, as a result of which ovulation is inhibited, and the synthesis of estrogens is reduced by almost 2 times [4].

Mastodynia has been described as a side effect of oral contraceptives [311]. In a study by G. Davies et al. in 16% of patients, mastalgia developed while taking estrogens and in 32% - while taking combined oral contraceptives (COCs). Changes in the mammary glands in women receiving hormone therapy were objectified in the study by E. Lundstrom et al., Who demonstrated an increase in breast density according to mammography in 54% of patients receiving continuous hormone replacement therapy, in 13% - against the background of cyclic hormone replacement COC therapy and in 18% - against the background of pure estrogen therapy. At the same time, according to D. Ader et al., The use of COCs reduces the frequency and severity of cyclic mastalgia [1].

Many researchers recognize that correctly selected low-dose hormonal contraception has a therapeutic and prophylactic effect in relation to mastopathy. The mechanism of action of combined oral contraceptives (COCs) includes suppression of the gonadotropic function of the pituitary gland by inhibiting the production of releasing hormones synthesized by the hypothalamus, which leads to inhibition of ovulation. The direct inhibitory effect of COCs on ovarian function has also been proven, the secretion of estrogen is reduced by almost 2 times. Symptoms of mastopathy often decrease or even completely disappear within the first two months of taking COCs, while a progressive decrease in the frequency (40%) of FCM is observed. In the United States, the use of hormonal contraceptives annually prevents 20,000 women from hospitalizing for mastopathy. It is considered established that, by reducing the incidence of benign breast diseases, hormonal contraceptives reduce the risk of breast cancer by 2 times [18].

In 2016, a meta-analysis of MEDLINE, EMBASE, Cochrane Database and Scopus publications was published to assess the impact of various progestogens on breast cancer risk. As a result, it was confirmed that the use of estrogens with progestogens is associated with a lower risk of breast cancer compared to synthetic progestogens [29].

Topical Drugs

1.Non-hormonal drugs. Recently, in the treatment of mastopathy, interest in local therapy has increased. This is due to the fact that in a number of cases a drug delivered directly to the mammary gland has the maximum therapeutic effect with minimal side effects on the body as a whole. A variety of local therapy for mastopathy is physiotherapy [16].

N.A. Ognerubov widely uses dimethyl sulfoxide as a drug for local therapy. This drug has anti-inflammatory, local anesthetic, diuretic, and vasodilatory properties. It should be used in the form of applications in a ratio with water 1: 2, 1: 3, 1: 4 (depending on tolerance). 15 - 20 procedures are planned for the course of treatment. In cases of severe pain syndrome, it is recommended to add 2-4 ml of 50% sodium metamizole solution and 2 ml of 1% diphenhydramine solution to dimethyl sulfoxide.

Hormonal drugs. The drug "Progestogel" (laboratory Besins - Incovesko, France) is a gel containing natural progesterone, in the amount of 1.0 progesterone per 100 g of gel. This is a topical preparation for percutaneous application on the breast area. Skin applications are used to increase the concentration of natural progesterone in the breast tissue. Acting on the state of the epithelium and the vascular network, "Progestogel" does not affect the level of progesterone in the blood plasma, and the concentration of the hormone in the tissue is 10 times higher than in the systemic circulation, which makes it possible to reduce the applied dose of the drug in comparison with the oral route. The subcutaneous location of the mammary gland determines the advantages of using this type of therapy. The drug is prescribed 2.5 g of gel on the skin of each breast 1 or 2 times a day continuously or from the 16th to the 25th days of the menstrual cycle in a cyclic mode. Indications for the use of the drug: mastopathy and mastalgia due to various reasons (taking oral contraceptives, hormone replacement therapy, impaired endogenous secretion of hormones, etc.). No contraindications to the use of Progestogel have been identified. Local application of the progesterone gel makes it possible to avoid many unnecessary surgical procedures to remove cysts [29]. In a cohort epidemiological study, long-term concomitant therapy with oral and transdermal progesterone reduced the risk of breast cancer [4].

Forms of mastopathy and their conservative treatment

Forms mastopathy	Etiological factors	Treatment
Mastodynia (mastalgia) at puberty	Hyperestrogenism (relative or absolute). Excessive synthesis of prostaglandins	Local progestins (Progestogel) or systemic action (Dyufaston, Utrozhestan). Inhibitors of prostaglandin synthesis (Nimesulide, Nise, topically 1% Diclofenac gel). Under constitutional hyperandrogenism - Diana-35 (4-8 courses). Vitamin therapy. Mastodinon
Mastodynia in perimenopause	Hyperestrogenism relative. Lack of progestins. Level up extragonadal estrogens (estrone). Increased FSH and LH levels	Progestogens internally and locally. nhibitors of gonadotropic hormones. Antiestrogens. Hepatotropic drugs. ith hypoestrogenism - phytoestrogens (Klimadinon). In the absence of menstruation - antiestrogens: Fareston (Toremifen). Indinol
Cystic forms of mastopathy	Hyperestrogenism. Hyperprolactinemia. Increased levels of FSH and corticosteroids. Low levels of progesterone, aldosterone. Hypothyroidism or euthyroidism. Hepatopathy, cholestasis. Diseases of the genital area (inflammatory, ovarian cysts, anovulatory cycle). Psychoemotional tension	Complexes of vitamins. Normalization of sexual activity. Sedatives. Hepatotropic and choleretic drugs. Enzyme therapy. Thyroid hormones. Dehydration. Progestins (Utrozhestan, Provera), especially with ovarian cysts. Phytopreparations (Mastodinon, Cyclodinon). Antiprolactins (Parlodel, Dostinex, Cabergoline), indicated for ovarian cysts. With a high level of FSH and LH - inhibitors of the gonadotropic function of the pituitary gland (Danazol). With a significant increase in LH levels - Zoladex, Dipherelin in combination with Fareston or Nolvadex (to avoid the "flash effect" - hyperestrogenism)
Mastopathy with a predominance of the fibrous component	Lack of progesterone and estrogens. Decrease in level corticosteroids. Hyperthyroidism. Hypo-, oligo-, amenorrhea	Regulation of hormonal balance. Reduction of hypoxic phenomena in the mammary glands. Herbal medicine (Mastodinon, Cyclodinon). Combined oral contraceptives

Preventive actions.

- Primary prevention should be aimed at eliminating causative factors, which implies:
- a healthy lifestyle (rational nutrition, correction of the psychoemotional state, the fight against physical inactivity, smoking cessation and alcohol consumption);
- Choosing a bra. Women with a cyclical or persistent form of mastalgia should pay special attention to this item of women's toiletry, since completely ignoring it, wearing a bra of an inappropriate shape or size can cause chronic deformity of the breast, its compression or overload of the ligamentous apparatus, especially in women with a large

and lowered breast [16].

- multiple births and full breastfeeding;
- treatment of gynecological diseases;
- treatment of endocrinological diseases and liver pathology.

Secondary prevention of various forms of mastopathy is reduced to early diagnosis. For these purposes, every woman, starting from the age of 18, must monthly perform the examination of the mammary glands itself and carry out instrumental research methods, as mentioned above [9, 20, 34].

Screening. An annual ultrasound of the mammary glands should be performed for women under 35 years old, then according to indications; X-ray mammography - for patients aged 35-50 years with a frequency of 1 time in 2 years, over 50 years old - annually.

CONCLUSION

Thus, there are many tools for the treatment of diffuse benign breast pathology. But it must be remembered that the success of treatment is due, first of all, to a thorough examination of the woman, including clinical, ultrasound, radiological research methods; individual choice of the method of therapy.

Prevention of breast diseases is extremely important, including prevention of abortions, especially repeated ones; timely treatment of gynecological diseases; rational contraception; early detection of breast pathology; correct management of pregnancy, childbirth and the postpartum period. In the management of patients with breast diseases, an important role is played by the continuity between doctors of various specialties (obstetricians - gynecologists, mammologists, surgeons, oncologists).

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