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TO THE ISSUE OF DISTRIBUTION AND MODERN PHARMACOCORECTION OF MASTOPATHY IN UKRAINE AND THE WORLD: REVIEW

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Abstract

Malignant diseases of the mammary glands are 3-5 times more common on the background of benign neoplasms of the mammary glands, and in 30 % of cases - on the background of nodular forms of mastopathy with the phenomena of proliferation.

This scientific review examines the etiology, prevalence of mastopathy in the world, approaches to its classification. The comparative analysis of diagnostic signs of nodular and diffuse mastopathy, strategic directions of pharmacocorrection are outlined.

The study was performed by bibliosemantic analysis of domestic and foreign literature sources that highlight scientific data on the stated problem.

Keywords: *mastopathy, therapeutic strategy, pharmacocorrection*

Introduction

Over the past 20 years, the incidence of breast cancer has increased by an average of 40 %, and the pathology has become the most common cancer, affecting every tenth woman aged 13 to 90 years.

Recently, the approach to the treatment of precancerous diseases is gradually changing, due to the emergence of a new unique and promising direction –"targeted therapy", based on the principles of targeted impact on the fundamental molecular mechanisms of a disease.

Given the polyetiology of the disease, the scheme of pharacocorrection of mastopathy requires a comprehensive approach using drugs of combined action: hormonal correction, anti-inflammatory drugs, resorbing agents, hepatoprotectors, sedatives and elimination drugs of synthetic and natural origin.

The objective of this study is to summarize and systematize the data of bibliosemantic analysis of the scientific literature on the issue of the distribution and modern approaches to pharmacotherapy of mastopathy in Ukraine and in the world.

Methods

The methodological approach to determining the target literature was based on the methodology proposed by Arskey & O'Malley (2005).

The research was conducted on the basis of data from such electronic databases as Google (Google Scholar); Medline; PubMed; ResearchGate; The Vernadsky National Library of Ukraine.

Results and Discussion

According to the WHO (1984), "... mastopathy is a fibrocystic disease with a violation of the ratio of epithelial and connective tissue components, various proliferative and regressive changes in breast tissue". Mastopathy was firstly described as a separate nosological unit by the surgeon and anatomist Sir Astley P. Cooper in 1829, but views on the etiology and pathogenesis of this disease are still very contradictory.

According to experts from the National Cancer Institute, the diagnosis of breast cancer (BC) may become a reality for almost 17% of Ukrainian women by the end of 2020, which gives reason to consider it as a socially significant epidemiological problem. According to the International Agency for Research on Cancer (IARC) at the WHO, more than 1.7 million women are diagnosed with BC each year. In Ukraine, according to the National Cancer Registry, in 2013, BC was firstly detected in 16,624 women (in 2012 – in 16,560), which is 72.2 cases per 100 thousand women in the country. Globally, mortality from this disease is becoming more frequent and kills more than 500,000 women worldwide each year. In Ukraine in 2013 7429 women with this diagnosis died (in 2012 - 7558) [1, 7, 12, 33, 41, 42].

Unified classification of mammary gland pathology, including fibrocystic mastopathy, is given in sections N60-N64 of the International Statistical Classification of Diseases (ICD – 10), which allows to compare the prevalence of this pathology in different regions of the world.

According to the International Classification of Diseases (ICD – 10), the term "mastopathy" refers to a group of dyshormonal benign dysplasias of the mammary glands with tissue hyperplasia, and the group of benign dysplasias of the mammary glands encoded by index N60 includes diffuse cystic mastopathy, fibroasledostosis, fibrotaledenosis, fibrotaledenosis, and unspecified benign dysplasia.

Clinically, there are two forms of mastopathy: nodular (peak incidence occurs at the age of 30-50 years) and diffuse. Nodules in the mammary glands can be single or multiple, in one or both glands, isolated or even on the background of diffuse mastopathy. Mastopathy is usually predisposed to women of reproductive age [32, 38].

According to the clinical and radiological classification of mastopathy by N. I. Rozhkova five forms of diffuse mastopathy are distinguished [43, 44, 49] (Fig. 1).

According to the classification of W. Dupont and DL Page (1985) the following histological types of mastopathy are distinguished (Fig. 2).

According to this classification, carcinoma "in situ", which is an invasive cancer, methodologically belongs to the group of precancerous pathologies [8, 37].

Non-proliferative forms of mastopathy include simple and complex cysts. In the group of proliferative mastopathy without atypia, a number of types are distinguished (Fig. 3).

Fibrocystic mastopathy (FCM) is the most common among women aged 20-50 years, half of whom have clinical symptoms. The pathogenesis of the disease is based on an imbalance of progesterone and estrogen. It is also important to increase the content of prolactin in the blood, which stimulates the proliferation of the ductal epithelium, as well as increases the expression of estrogen receptors. In addition, hyperprolactinemia leads to suppression of phase II of the menstrual cycle and progesterone deficiency. Clinically, FCM may be manifested by bilateral cyclic pain, swelling and heaviness in the mammary glands, increased density (viscosity / nodularity) of tissues on palpation. Visually, roughness of the skin can be determined over the areas of seals. Sometimes women are bothered by periodic sudden discharge from the nipple. No association between complex PCM and BC development was identified [14, 21, 29, 45, 46].

Breast cysts are cavities filled with fluid and covered with epithelium. The formation of cysts occurs under the influence of ovarian hormones, which explains their sudden onset, accelerated growth during menstruation and spontaneous regression after the cycle. These lesions are more common in women over the age of 35 and rarely occur before the age of 25. The likelihood of cysts decreases after menopause. A characteristic diagnostic sign during mammography is the absence of calcium salt deposits. In order to analyze the cystic components, a puncture fine-needle aspiration biopsy is performed. Depending on the nature of the fluid obtained, there are three variants of cysts: a simple cyst – filled with clear or green fluid; milk cyst (galactocele); blood cyst (high probability of malignancy) [3].

Treatment tactics are determined based on biopsy results.

Fibroadenoma is a well-defined, motile, benign tumor of the breast, consisting of stroma and epithelium. This type of tumor is more common in women under 30 years of age. Fine-needle aspiration puncture biopsy or histological examination of the excised tumor is used for diagnosis. At the sizes of a fibroadenoma less than 2-3 cm and age of the patient younger than 35 years it is possible to be limited to dynamic supervision [11, 30].

Complex fibroadenomas are characterized by such proliferative changes as sclerotic adenosis, duct hyperplasia and deposition of calcium salts in epithelial tissues. The presence of these tumors is associated with a slightly increased risk of cancer.

Leaf-like (phylloid) tumors are large fibroadenomas that grow rapidly. In 25 % of cases they are malignant, in 10 % they are able to metastasize.

Sclerotic adenosis occurs due to the proliferation of acinuses in the lobes without damage to the surrounding stroma, but with the involvement of ducts. This form of mastopathy is a high risk factor for BC development [2, 13].

Papilloma is a benign neoplasm of the breast that forms from the epithelial tissue of the excretory ducts. Most papillomas are located under the areola. If the formation is under the nipple and areolar complex, it can cause bloody discharge from the nipple. Treatment consists in its complete removal by means of a near-areolar incision. Invasive papillary carcinoma should be ruled out before surgery [31, 37].

Ectasia of the mammary duct is more common in elderly women in the subareolar area. Characteristic signs of the disease are pain in the breast, retroareolar compaction, itching and burning in the nipples, discharge from the nipple (from whitish to brown and bloody).

Fat necrosis is associated with trauma or radiation to the breast. Lipid-filled macrophages, scar tissue, and chronic inflammation cells are detected during diagnostic biopsy.

The group of mastopathies also includes gynecomastia – a pathological enlargement of the breasts in men. This condition occurs in 50-70 % of healthy adolescents (pubertal form) and 40 % of aging men. Gynecomastia is manifested by compaction and enlargement of the glands, a feeling of heaviness and pain on palpation [39].

In boys (prepubertal form), gynecomastia may be a manifestation of adrenal carcinoma or testicular carcinoma. In adult men, the pathology may be associated with the use of certain drugs (steroids, digitalis, spironolactone, antidepressants).

In addition, diagnoses is made on the results of the biopsy according to the histological classification of breast tumors (WHO, 1995). Morphologically there are distinguished non-proliferative and proliferative forms of benign dysplasia. In the non-proliferative form, the main changes occur in the ligaments and connective tissue of the breast. The proliferative process is associated with an increase in the mass of glandular tissue, the appearance of areas of adenosis, dilation and branching of the ducts of the breast. Most often, in practice, a non-proliferative form is observed. According to various estimates, the proliferative form is registered in 6–25 % of patients [42].

One of the symptoms of benign breast disease is mastalgia (mastodynia). According to the nature of the occurrence, there are cyclic (occurs regularly, associated with the phases of the menstrual cycle) and non-cyclic (develops without a certain frequency) mastodynia. If the pain is concentrated in one area, BC should be ruled out [10, 23].

Pain is the most common reason for seeing a mammologist. The woman is often referred to a doctor by the associated carcinophobia. It is important that mastalgia can not be considered a pathognomonic symptom of a non-proliferative form of benign breast dysplasia (BBD): pain in the mammary glands is possible in the case of other benign diseases in cancer of this location. The connection between mastalgia and BC has recently been resolved positively. For example, in 10 years of a study conducted in Edinburgh among involving 8,504 patients with chest pain as the main complaint 4.6 % were diagnosed with BC [22, 25, 27].

Cyclic mastalgia for 37 months. increases the risk of BC by 5 times and can play the role of an independent factor.

From a clinical point of view, it is extremely important that the risk of BC in women with mastopathy depends on the nature of the proliferative process. The actual precancerous conditions include proliferative forms of mastopathy with hyperplastic epithelial growth and dysplasia. The most unfavorable in terms of prognosis atypical ductal or lobular proliferation. In order to detect it, microscopic differential diagnosis is required [9, 16, 47].

The greatest achievement of theoretical oncology in the second half of XX century. was the disclosure of the role of chronic inflammation as a precancerous condition. In the case of chronic inflammation, stem cells begin to proliferate, transforming into malignant tumor stem cells. "Inflammatory cells" secrete growth factors for tumor cells, as well as angiogenic factors that stimulate the formation in the tumor of the microcirculatory tract. As a result of chronic inflammation, a stroma of a malignant tumor is formed. Permanent inflammation due to permanent necrosis in the tumor provides cells with angiostimulatory and growth factors.

The path from the origin of the tumor cell to the progression of the disease is determined by the consistent implementation of the patterns inherent in tumor growth (carcinogenesis). It is common to characterize the development of cancer in the form of four successive stages: initiation, promotion, avoidance of differentiation and progression [6, 48].

The most studied physiological promoters of proliferation in the breast today are the steroid ovarian hormone estradiol and its metabolites.

Homeostasis of breast tissue is the result of a balance between proliferation, differentiation and apoptosis of its cellular composition, which depends on the optimal ratio in both serum and breast tissue, the concentration of major sex hormones (estrogen and progesterone), which provide the above effects.

A significant step in a comprehensive approach to reducing the incidence of BC was a unified clinical protocol "Breast Cancer" (Order of the Ministry of Health of Ukraine № 396 dated June 30, 2015), in which mastopathy is organizationally classified as a precancerous pathology to be detected in mammological screening programs (physical, ultrasound and radiological with histological

verification of the nature of the process in case of suspected BC), and women with any form of mastopathy are subject to mandatory treatment [42].

Recently, the approach to the treatment of precancerous diseases is gradually changing, due to the emergence of a new unique and promising direction – target therapy, based on the principles of targeted impact on the fundamental molecular mechanisms underlying a disease [40].

In the treatment of BC there are used several main classes of targeted drugs that provide control of the cell cycle: 1) affect cellular estrogen receptors; 2) inhibit aromatase; 3) block the receptor of human epidermal growth factor; 2 (HER; 2) and PARP.

According to the Recommendation of the National Integrated Cancer Network of the United States 2017, BC occupies a leading position in the structure of cancer morbidity and mortality of women in most countries, including Ukraine. In general, in our country, the detection of BC during preventive examinations remains low, and the rate of onset (III-IV degree), which is the main criterion for the quality of diagnosis, on the contrary, is high. This determines the relevance of the introduction of early and sometimes preclinical diagnosis, as well as the importance of finding and developing new methods of antitumor treatment. [1].

In Russia in 2013, the incidence of BC was 320 per 100,000 population, ie about 0.008 % of the female population annually. In 741 Ghanaian women (mainly aged 38.6 years) who sought mammological care in 2001-2004, mastalgia was the main symptom (50.2 %), with an average duration of pain of 11.3 ± 8,9) months. BC was diagnosed in 7.8 %, recurrent BC – in 0.8 % of patients. In other cases (over 88 %) mastalgia was associated with malignant transformation of breast tissue. This suggests that mastalgia cannot be considered a marker of cancerous transformation, but should be considered a significant risk factor. The correlation between the presence of mastodynia and the possible risk of BC becomes clearer given the differences in pain (cyclic and non-cyclic forms). In a study of the association between cyclic mastalgia and breast cancer involving 5,463 women, 28 % (1,529 patients) reported chest pain. At the same time, 15.8 % (861) were diagnosed with BC. It was found that in women with acyclic mastodynia the disease was less malignant than in the comparison group, regardless of age, reproductive phase and other risk factors for BC [29].

The results of a prospective cohort study conducted in France in 1976–1997 are significant. The authors analyzed the relationship between cyclic mastalgia and the likelihood of BC in untreated patients (n = 247). The mean follow-up period was (16 ± 5) years, 22 cases of malignant breast tumors were registered. The authors concluded that cyclic mastalgia lasting from 1 to 36 months. increases the risk of breast cancer by 2.9 times and a duration of 37 months. and more – 5.3 times. It is this form of mastodynia that can play the role of an independent marker that demonstrates an increased risk of breast cancer [2].

The results of global clinical studies suggest that the incidence of BC in women with mastopathy is extremely higher than in women with normal breast glands. According to research in 2007, the risk of BC is 4-37 times higher than the population in the fibrocystic form of mastopathy and 30-40 times higher in the nodular form.

Fibrocystic form of the disease is up to 30 % in the structure of BBD. At the same time, the connection with BC can be traced in 40.5 % of studies.

Modern technologies of oncological diagnostics allow to detect the disease at an early stage of malignancy and improve the prognosis of therapy, but do not affect the incidence. BC in the "in situ" stage with a careful diagnostic search can be suspected in 39 % of women aged 40-50 years, although only 1 % of women in this age group actually are diagnosed with BC.

During a thorough examination of 8 conditionally healthy patients who underwent reduction mammoplasty, 8.4 % had atypical lesions, 15 % had proliferative, and 57 % had non-proliferative breast lesions [20].

In 2015, clinical oncologists proposed an integrative model that could predict the risk of BC. The system takes into account many individual parameters (results of the first mammological

screening in combination with demographic and anamnestic risk factors), thus allowing to plan preventive measures and to actively observe patients with a high degree of risk [35, 37].

It is now known that malignant diseases of the mammary glands occur 3-5 times more often on the background of benign neoplasms of the mammary glands, in 30 % of cases – in nodular forms of mastopathy with the phenomena of proliferation. Therefore, in the fight against cancer, along with early diagnosis of malignant tumors is equally important timely detection and treatment of precancerous diseases.

Diagnosis of breast diseases is based on their examination, palpation, mammography, ultrasound, puncture of nodules, suspicious areas and cytological examination of the punctate.

Examination of the mammary glands in women of reproductive age should be performed in the first phase of the menstrual cycle (2-3 days after menstruation), because in the second phase due to coarsening of the glands there is a high probability of diagnostic errors (S. S. Chystyakov et al., 2003).

Thus, against the background of the prevalence of mastopathy in the world and the existence of a high risk of malignant neoplasms in breast tissue, we can say that the problem of comprehensive and timely treatment is urgent and globally significant, and the development of new original safe drugs is a very important issue.

Early diagnosis can prevent up to 80 % of annual cancer deaths. Cancer prevention is a reality in high-health countries.

V. I. Kulakov and co-authors (2003) used wobenzyme and phytotherapy in the treatment of patients with various forms of mastopathy accompanied by mastalgia. The effectiveness of mastalgia treatment after 3 months was 65 %. Many studies are devoted to the treatment of this pathology, but the problem remains relevant today (L. N. Sydorenko, 1991; T. T. Tahiyeva, 2000).

In order to study the question of the precursors of increased risk of malignant neoplasms of breast tissue, 9087 women with benign breast diseases were studied. This group was observed for an average of 15 years, during which period 707 cases of BC developed, which is one of the largest such studies of its kind.

Retrospective and prospective studies showed a relative risk of BC from 1.5 to 1.6 in women with benign breast disease compared to women in the general population [18, 19].

The median survival of women with BC has increased significantly in recent years, mainly due to the introduction of population screening programs and adjuvant treatment. Much progress has also been made in the treatment of disseminated forms of BC [24].

Along with this, strategic cancer indicators in different countries and on different continents differ significantly. The best survival results were obtained not through the use of new therapeutic strategies, but as a result of preventive measures at the state level.

The concept of oncology development within the state program in Ukraine envisages screening and prevention as the main priority areas during the reform of the country's health care system [36].

From 2007 to 2016, the national program to combat cancer in Ukraine had the force of law. For the period 2017–2022, the concept of a new program was developed, which aims to reduce society's losses from cancer by reducing cancer morbidity and mortality through interdisciplinary measures for prevention, early detection, comprehensive treatment and rehabilitation of cancer patients.

The concept of the new Oncology program, which was approved by the Congress of Oncologists of the country in May 2016, includes the following tasks (Fig. 4).

Priority areas of cancer control in Ukraine are shown in Fig. 5.

The EU guidelines for cancer screening programs cover three sites: rectal and colon cancer (men and women should be involved from the age of 50), cervical cancer (women should be involved from the age of 28) and breast cancer (women should be involved). from 50 years) [28].

The main tool for breast cancer screening is mammography. There are such new technologies as

3D tomosynthesis, MRI, positron emission tomography of the breast, SmartBra, iBreastExam, but their importance in preventive oncology has yet to be determined. The main problem with the implementation of population screening in Ukraine is not the lack of tools, but the lack of a clear organizational system for this part of preventive medicine. To date, it was not determined who should compile the database of the population involved in the screening (this should take into account the law on non-disclosure of confidential data); on the basis of which medical institutions it is necessary to conduct screening tests; how to do in case of false-positive and false-negative results of these tests; who will be responsible for carrying out specific diagnostics and treatment of the revealed pathology. Finally, who will pay for the screening of the motivating part of the population: the state, insurance companies or the participant in the screening process [5].

Given that the number of patients with pre-neoplastic pathology (benign mastopathy) that inevitably increase during the implementation of preventive mammography screening programs, methods of treatment of this group of patients should be available in public health care institutions.

The US Preventive Services Task Force (USPSTF) reviewed the role of effective breast cancer screening in reducing mortality from it, its prevalence, and treatment-related morbidity; harmfulness of breast cancer screening; the role of testing the performance of digital mammary tomosynthesis as the main screening strategy and additional screening in women with high breast tissue density. In addition, the USPSTF considered comparative decision-making models for the optimal age of onset and end and intervals for mammography screening; investigated the increase in breast tissue density as a risk of cancer, analyzed the extent to which concomitant pathologies affect the benefit-harm ratio of screening mammography [15].

These recommendations apply to asymptomatic women 40 years of age and older who do not have BC or have been previously diagnosed with high-risk breast cancer and who are not at high risk for BC due to a known genetic mutation (eg BRCA1 or BRCA2 gene mutation or other familial BC syndrome). or chest irradiation at a young age.

Important questions remain about the degree of risk associated with common non-proliferative benign tumors and the extent to which a family history affects the risk of developing BC in women with proliferative or atypical lesions. DuPont and Paige found that women with non-proliferative disease did not have an increased risk of late BC. In an additional study conducted within the National Breast Cancer Surgical Adjuvant Treatment Project (NSABP) for BC, in contrast, a relative risk of 1.6 was found for women diagnosed with "lower-grade benign breast disease." A limitation of the NSABP study, however, was the lack of a central pathological examination [26].

Other studies by DuPont and Paige showed that women with atypia and family history had an 11-fold higher risk than women with non-proliferative lesions and no family history [2, 18].

Hereditary forms account for 5–10 % of BC cases, 30 % of which are caused by mutations in the BRCA 1/2 genes. The prevalence of VRCA mutations is approximately 1 case per 250 women.

According to the recommendations of a number of medical associations, the determination of mutations in the BPA gene is performed in the following cases:

- more than three cases of BC or ovarian cancer in the family;
- more than one case of BC or ovarian cancer in a family of women under the age of 50;
- the presence of BC and ovarian cancer in the same woman;
- BC at an early age;
- BC in men.

The current panel of genetic tests includes the study of not one mutated BRCA gene, but 25 high- and low-penetration genes to identify mutations that cause cancer in different locations: BC, ovaries, endometrium, colon and rectum, stomach, pancreas, prostate.

In the 1980s, sociologists, feminists, and some oncologists expressed concern about the rapid

commercialization and possible negative psychological consequences of genetic testing. Studies in subsequent years showed that the psychological consequences of genetic testing did not lead to increased anxiety or depression in women, and preventive measures at high risk of hereditary cancer (active surveillance, chemoprophylaxis or prophylactic mastectomy) was very effective [24].

The USPSTF recommends that mammograms should be performed every two years for women between the ages of 50 and 74. The decision to start mammography screening in women under the age of 50 should be individual. Women who value the potential benefits more than the potential harms can begin two-year screening between the ages of 40 and 49. The USPSTF concluded that the available data were insufficient to assess the balance of benefits and harms of screening mammography in women 75 years of age and older.

Benign breast disease is an important risk factor for late BC, which can develop in any breast. It covers a range of histological lesions, usually divided into non-proliferative lesions, non-atypical proliferative lesions, and atypical hyperplasia, with an increased risk of BC associated with proliferative or atypical lesions. Recognition of benign breast disease became widespread as mammography expanded, so accurate risk assessments for women receiving this diagnosis are a must.

Measures to reduce the incidence and mortality from BC in Ukraine are in the field of preventive medicine: in the organization of population screening programs, medical and genetic counseling and genetic testing for burdensome family history, as well as in the treatment of precancerous breast pathology in women at high risk of invasive cancer [17, 24].

The review of the updated version (2017) of the leadership of the National Comprehensive Cancer Network (NCCN) of the United States measures to reduce the risk of BC are provided.

The Claus model must consider the presence of BC in one or two relatives of the first or second degree of relationship and the age at which they were diagnosed with BC. Appropriate models were used for the research: Brcapro, Boadicea and Tyrer-Cuzick model.

Brcapro – a statistical model with appropriate software that allows you to assess the risk of mutation BRCA1 / 2; based on the burden of hereditary history (BC, ovarian cancer), including BC in men and bilateral disease.

Boadicea is a model for calculating the risk of breast cancer and ovarian cancer, as well as the possibility of BRCA mutations 1/2. The model uses information about aggravated heredity (breast cancer, ovarian cancer, prostate cancer, pancreas), the age of diagnosis of malignant neoplasms of these localizations in relatives, information about the age of relatives without oncopathology and nationality [4, 7].

Tyrer-Cuzick model – is an assessment of the risk of BC, the probability of BRCA mutation 1/2. It contains a wide range of questions: age, height, weight, age of menarche and menopause, hormone replacement therapy, age of first childbirth, burdened heredity (BC, ovarian cancer); presence in the anamnesis of the tested atypical breast hyperplasia, LCIS, ovarian cancer.

The results of the risk assessment of BC are given in table 1.

To reduce the risk of breast cancer, the management of the National Integrated Cancer Network (NCC) proposes the following measures:

- genetic counseling of patients at high risk due to a burdensome family history or very early development of BC / ovarian cancer (see NCCN guidelines for assessing the high genetic / family risk of BC and ovarian cancer);
- healthy lifestyle;
- consideration of the risks of BC associated with the use of combination estrogen-progesterone therapy lasting ≥ 3-5 years;
- limiting alcohol consumption to less than 1 serving of beverage / day (1 serving of alcoholic beverage = 10–12 g of alcohol; this is 1 glass of vodka or cognac (25–30 ml), or 1 glass of wine (100–120 ml), or 1 small mug of beer (220-260 ml);
- performing physical activities;

- weight control;
- breastfeeding;
- therapeutic agents that reduce the risk of breast cancer;
- consideration of mastectomy with preservation of the nipple-areolar complex to reduce the risk of cancer. The operation is a total mastectomy with preservation of the nipple / areola and breast skin. Efforts should be made to minimize the amount of residual breast tissue;
- the opportunity to participate in clinical trials for screening, risk assessment and other surgical interventions that reduce the risk of cancer. Mastopathy is mostly a hormone-dependent pathology, its treatment should begin with treatment of the underlying endocrine disease. In case of hyperprolactinemia or normoprolactinemic galactorrhea, in particular in case of pregnancy planning, dopamine agonists should be used in modern conditions. These drugs belong to the class of evidence A, i.e. to drugs with proven efficacy.

According to the results of the Cochrane Review (2009), drugs for the conservative treatment of BBT are divided into several categories:

- evidence of class A – definitely effective (dopamine receptor agonists, antiestrogens (tamoxifen), testosterone derivatives, phytoestrogens);
- evidence of class B – probably effective (combined oral contraceptives, progestogens, gonadotropin-releasing hormone agonists, nonsteroidal anti-inflammatory drugs);
- evidence of class C – probably ineffective (vitamin E, diuretics) [5, 34].

Therefore, self-treatment of mastopathy is impossible, and at the slightest suspicion of the disease it is necessary to urgently consult a specialist. Treatment of mastopathy requires comprehensive approaches due to the polyetiology and polysymptomatic nature of the disease.

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Table 1. The degree of risk of breast cancer

Localization of cancer	Age period	Risk of cancer in individuals with a mutation, %	Risk in the general population, %
The degree of risk of cancer due to mutation BRCA 1			
Female breast	Up to 50 years	≤ 51	1.9
	Up to 70 years	≤ 87	7.3
	The second primary tumor within 5 years after diagnosis	≤ 20	2
Ovaries	Up to 50 years	≤ 23	0.2
	Up to 70 years	≤ 44	0.7
	The second primary tumor within 5 years after diagnosis	≤ 12.7	<1
The degree of risk of cancer due to mutation BRCA 2			
Female breast	Up to 50 years	≤ 28	1.9
	Up to 70 years	≤ 84	7.3
	The second primary tumor within 5 years after diagnosis	≤ 12	2
Ovaries	Up to 70 years	≤ 27	0.7
	The second primary tumor within 5 years after diagnosis	6.8	<1

Figure 1. Forms of diffuse mastopathy

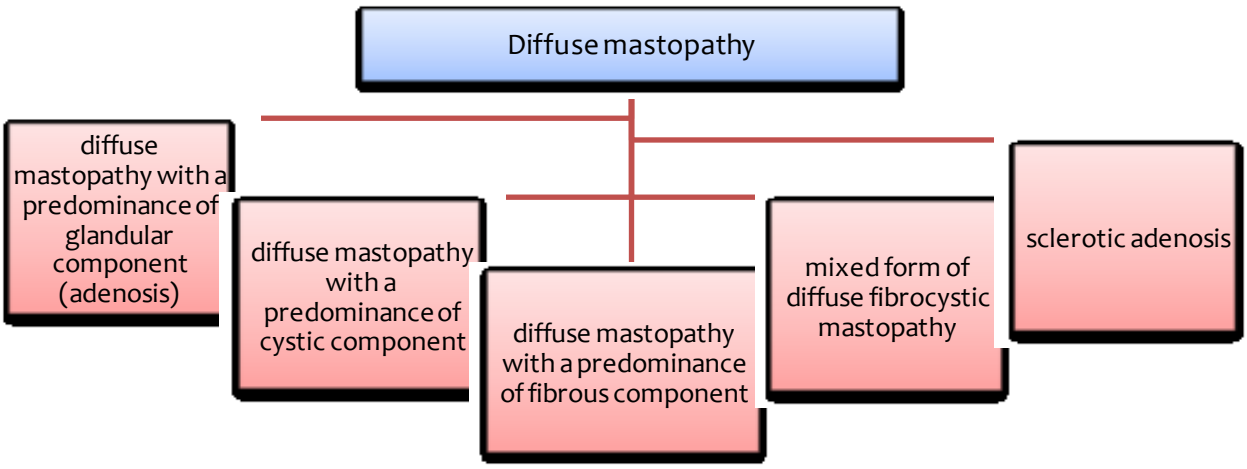

Figure 2. Histological types of mastopathy

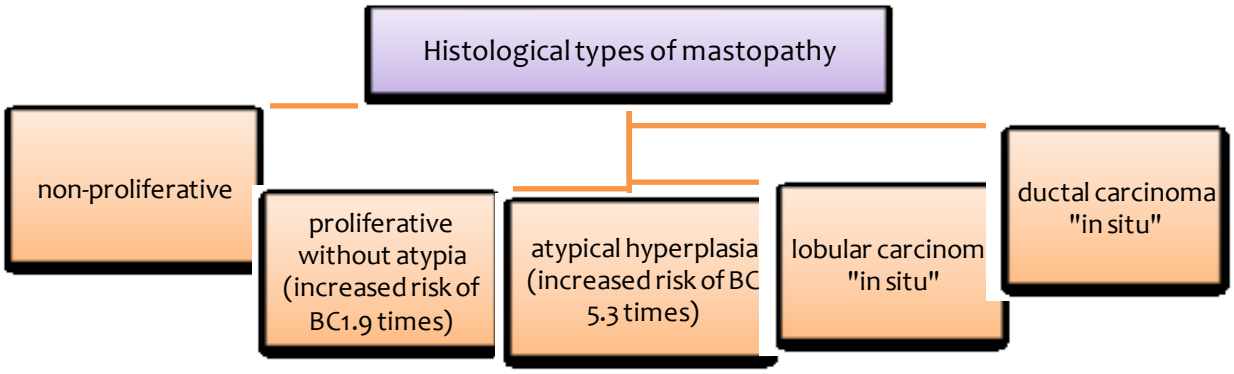

Figure 3. Types of proliferative mastopathy without atypia

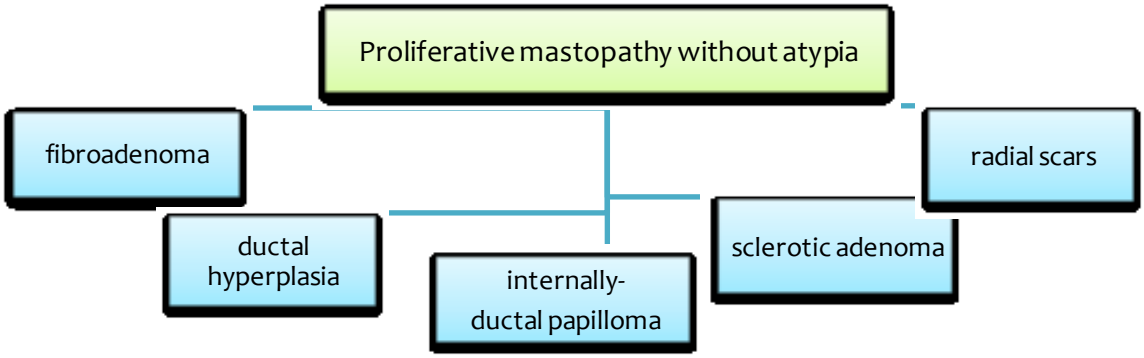

Figure 4. The concept of the program "Oncology"

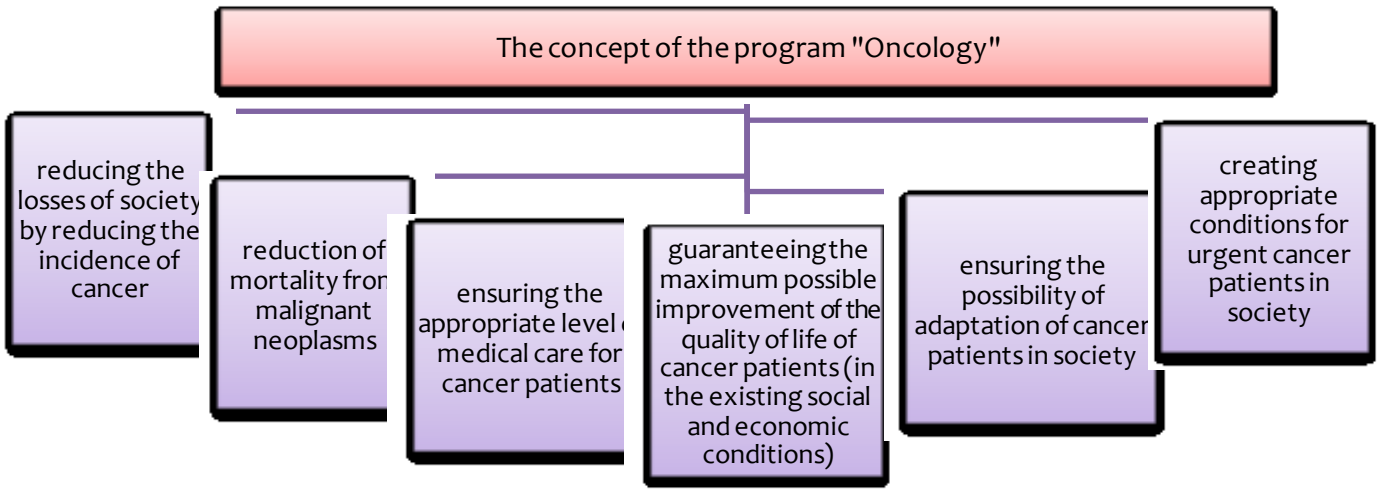

Figure 5. Priority areas of cancer control in Ukraine