

SECTION 4. PHARMACY

4.1 Pharmaceutical aspects of women's reproductive health

One of the main and priority tasks of the World Health Organization (WHO) is the health of women during pregnancy, because it depends on the state and quality of health of future generations [155, 156].

Nowadays, due to the decline in the quality of life of people, which is related to the deteriorating environmental situation and economic troubles, there are negative trends in population health and the deepening demographic crisis. The state of reproductive health is of particular concern, which is a necessary part of the health of the nation as a whole and ensures the continued existence and development of society. According to the Ministry of Health of Ukraine, disorders of women's reproductive health account for 15-20% of all diseases, including death and disability [157].

In the field of women's reproductive health the inflammatory problems of female genitals representing the whole spectrum of diseases of a tract remain an actual problem [157, 158]. Number of inflammatory diseases of the female genital organs tends to increase and accounts for 13 - 25% of all diseases of the reproductive system [157-160].

Inflammatory diseases of the female genital organs include various nosological forms. Today, pelvic inflammatory disease (PID) accounts for 60% of the total number of gynecological nosologies [160]. According to the localization of the inflammatory process, it is divided into diseases of the lower (vulvitis, vulvovaginitis, endo- and exocervicitis, colpitis etc.) and upper genital tract (endometritis, salpingo-oophoritis, parametritis, perimetritis etc.) [158].

The authors research [157] noticed a change in the origin of the inflammatory process: from 1990 to 2000, acute forms of salpingoophoritis predominated (67%), and from 2000 to 2020 - exacerbation of chronic inflammatory process (74,5%) became the predominant form.

The quality of life of a pregnant woman is a worldwide core value both in a holistic sense and in a social aspect, which includes the possibility of ensuring a standard of living that is necessary for a successful pregnancy and, if necessary, the possibility of applying for pharmaceutical care.

Ukraine, like other European countries, has a very low birth rate. The economic and social consequences of the demographic decline in the birth rate is a problem that can be solved by developing a harmonized with European and international legislation regulatory and technical framework governing medical and pharmaceutical activities.

Family planning is one of the human rights. Ukraine, like most countries in the world, has signed major declarations and other international human rights instruments, which guarantee the right of women to receive adequate medical care based on information, counseling and family planning services, the right of the child to a healthy and desirable birth, and the right of married couples to independently and consciously decide how many, where and when to have children [161].

According to the WHO, family planning includes prevention of unwanted pregnancies, choice of time of birth of children depending on age, health status of parents, birth of only desired children.

Research on identifying priority ways to develop a national regulatory system in the field of medical and pharmaceutical care for women during pregnancy is one of the urgent and necessary tasks in the field of health care.

Nowadays, the institutional problems of the family are effectively addressed through a specially organized system of public policy on the family, women, children and youth. This is facilitated by legislative provision of favorable conditions for family development, effective implementation of its reproductive, educational, economic, social functions, observance in practice of the principle of equality of rights of women and men, implementation of targeted policies on youth employment, prevention of child neglect and begging, prevention of social orphanhood [162].

The World Health Organization (WHO) defines maternal death as «the death of a woman that occurred during pregnancy or within 42 days of its termination (regardless of its duration and location) for any reason related to the pregnancy, its

complications or pregnancy monitoring, but not from an accident or random causes» [163]. In 2019, the United States found that 754 women died from maternal mortality, compared to 658 in 2018.

To characterize maternal mortality, maternal mortality rate is important (the ratio of the number of maternal deaths to number of live births or total number of births (live births and stillbirths together) and the level or rate of maternal mortality (maternal deaths per 100,000 live births). Maternal mortality rate in 2019 (20.1 deaths per 100,000 live births) was significantly higher than in 2018 [164].

According to the Opendatabot portal, in 2020 Ukraine has the lowest birth rate in 10 years. It amounted to 293,457 people, while the death rate reached 616,835 people. In general, in 10 years the birth rate in Ukraine has decreased by 40% [165].

It should be noted that the reproductive system of women largely depends on gynecological health, degree of awareness of methods and means of contraception, culture of reproductive behavior [166].

Accumulated to date clinical and experimental experience in the use of drugs during pregnancy requires a comprehensive research, that takes into account not only safety but also the degree of organization and availability of pharmaceutical care for pregnant women at the state and regional levels.

Concept of development of pharmaceutical sector of healthcare industry of Ukraine provides for the solution of priority tasks on improving the availability and quality of health care, maintaining and strengthening health of the population, as well as maternity and childhood protection. The most important mechanism for implementation of this program task is the issue of population growth, which can be ensured by improving system of reproductive health [167].

Simultaneously, reform processes taking place in the field of health care in Ukraine require establishment of modern priorities and requirements for quality of pharmaceutical care, which requires appropriate changes in management approaches, procedures and methods [168].

Rational use of drugs during pregnancy is an important problem and at the same time remains one of the least studied. Relevance of improvement of pharmaceutical

care for diseases of pregnant women considering evidence data in accordance with requirements of Good Pharmacy Practice (GPP) and rational use of drugs requires evaluation of drugs prescribed to pregnant women, in terms of the principles of «medicalization», compliance with which ensures safety, rationality and effectiveness. A group of authors (Maksimovich N.M., Zaliska O.M., Kosyachenko K.L.) segmented drugs by safety categories according to FDA classification [169].

Strategy for maintaining health of pregnant women is also a priority for health care system. The UN «Millennium Development Goals» program has a theme «Improving maternal health and reducing child mortality» [170]. Optimization of medical supply for pregnant women is actual problem, that should be addressed in the near future.

Special significance in health care system of Ukraine is the protection of motherhood and childhood due to their importance for development of society and ensuring interests of every family or citizen. WHO defines: formation and preservation of reproductive health is key to quality implementation of reproductive right of every woman. Necessary components are: healthy lifestyle, sex education, prevention of sexually transmitted infections, family planning, pre-pregnancy training, quality services for monitoring pregnancy and childbirth, newborn care, motivated preventive dynamic monitoring of women, timely detection and treatment of gynecological diseases, prevention of oncogynecological pathology, which is achieved through the application of measures in the field of public health [171].

Modern organizational approaches recommended by WHO require adherence to quality of health care, which consists in ability of health care services, which contribute to improving quality of health of both individuals and groups of patients. To accomplish this task, health services need to be characterized by safety, efficiency, timeliness, efficiency, social justice and a focus on people's needs and interests.

In Ukraine, in the process of reforming health care system, constant attention is paid to solving the most pressing problems related to preservation of maternal and child health, reducing their mortality, morbidity and disability. At the stage of reforming

domestic medicine, there is also issue of maternal health care, which requires implementation of high-quality medical and pharmaceutical care.

These studies are especially important in context of reforming domestic health care system in direction of building socially oriented models of pharmaceutical supply and formation of appropriate legal and regulatory framework in implementation of compulsory health insurance, which is also gaining relevance.

Health of pregnant women in Ukraine is unsatisfactory due to trend of increasing morbidity, prevalence of diseases and disabilities. Process of depopulation, which has been observed in Ukraine since 1990, has become a demographic crisis, in which preservation of life and health of every pregnant woman is becoming extremely important nationwide [165].

Level of disability among children also remains high, which is one of the most unfavorable phenomena in the complex characterization of the state of health and social well-being of the population. Statistics data convincingly show the high prevalence of chronic pathology among pregnant women, and their health status can be described as catastrophic. Economic difficulties, reduced attention to social problems, continuous inadequate increase in the negative impact of environmental and medical and social risk factors, deteriorating nutrition, reducing the effectiveness of traditional preventive measures has led to this situation. These are just some of the problems that affect health of pregnant women, solution of which has a nationwide character. Ukraine, as a member of WHO, should take appropriate medical measures recognized by WHO as the most cost-effective. State health policy became the object of study of many scientists in pharmacy.

Organizational, informational and pharmacoeconomic studies of pharmaceutical care for various diseases in Ukraine were conducted by scientists such as D.S. Volokh [172, 173], M.S. Ponomarenko [174], A.A. Kotvitska [175] etc. Some pharmaceutical aspects of drug supply of pregnant women in hospital were studied by M.L. Syatin with co-authors [176], methods of pharmacoeconomic analysis at the risk of abortion processed by L.V. Yakovleva, O.V. Tkatchow [177].

Work of Kazimirova N.V. [178] is devoted to study of clinical course of pregnancy, childbirth, postpartum period and condition of newborns in women who used combined oral contraceptives (COCs) to plan their first pregnancy, which is confirmed by clinical and statistical development of pregnancy and childbirth. It has been proven that method of family planning provides most favorable result of first birth and makes it possible to justify the most optimal method of family planning and first pregnancy. Birth control, maintaining women's health, reducing maternal and perinatal mortality, gynecological morbidity, prevention of abortion-related complications are largely determined by effectiveness of modern contraceptives as an alternative to abortion (Kazimirova N.V.) [178].

Nowadays, the most effective and common methods of birth control are hormonal contraceptives, introduction of which into clinical practice has been possible since 1960 and is associated with names of American scientists G. Pincus and M. Garsid, who showed that hormonal contraceptives inhibit ovulation in 100% of women. Peculiarities of pregnancy and childbirth in women who used combined oral contraceptives of the III generation when planning first childbirth were revealed.

Therefore, hormonal contraceptives are highly effective means of preventing pregnancy. Arsenal of existing drugs is quite wide and allows individual selection of oral contraceptives (OC) taking into account health status, patient's desire, which significantly reduces incidence of adverse reactions and provides high acceptability of this contraceptive, thus contributes to family planning [178].

Gravchenko L.O. together with co-authors [179] conducted research on study of contraceptive market, treatment regimens and standards, behavior of end and intermediate (doctors) consumers for prevention and treatment of diseases of reproductive system in hospital, outpatient clinics for self-treatment of patients. Methodological approaches to the rational individualized choice and use of modern competitive contraceptives, introduction of assortment lists of contraceptives developed on the basis of evidence-based medicine and pharmacoeconomics, taking into account their affordability were developed [179].

It is no secret that use of modern methods of contraception has significant advantages over abortion. According to WHO, about 73 million artificial abortions are performed annually in world. Six out of ten unplanned pregnancies and 3 out of 10 pregnancies end in abortion. Statistics show that 45% of all artificial abortions are dangerous, 4,7 to 13,2% of maternal deaths per year can be classified as dangerous abortions [155].

Situation with abortions in Ukraine is considered by experts as ambiguous: high level of their prevalence is combined with tendency of a steady decrease in their number. According to Opendatabot portal, 163,668 abortions were registered in Ukraine in 2011 and 64,574 in 2020, which indicates a 2,5-fold reduction in the number of abortions [165].

Center for Medical Statistics of the Ministry of Health of Ukraine provides information that the total number of abortions as of 2020 – 61,048 cases: of which, spontaneous abortions – 10,744, which is 17,5%; unspecified (spontaneous abortions without criminal intervention, if the woman was not registered for pregnancy in a women's clinic) – 20,958 (34%); pregnancy, which was terminated before 12 weeks – 55,251 (90,5%); medical (legal) abortion during pregnancy for a period of 12 to 22 weeks – 1,246 (2%) [180].

In connection with existing abortion rates, Ukraine has moved from category of countries with a high prevalence (more than 20 abortions per 1000 women of fertile age (WFA)) to the category of countries with a medium prevalence (15 to 20 abortions per 1000 WFA). However, abortion in Ukraine remains one of the methods of birth control for a significant number of families - 2% of women of childbearing age [180].

The closest to Ukraine indicators are in China, the USA and Australia (Fig. 1). Herewith overpopulated China is pursuing a conscious policy of birth control. The United States and Australia are among the few developed countries that do not have demographic problems. Though countries of Western Europe have demographic difficulties, number of abortions per 1 woman is 3,5 to 7 times lower.

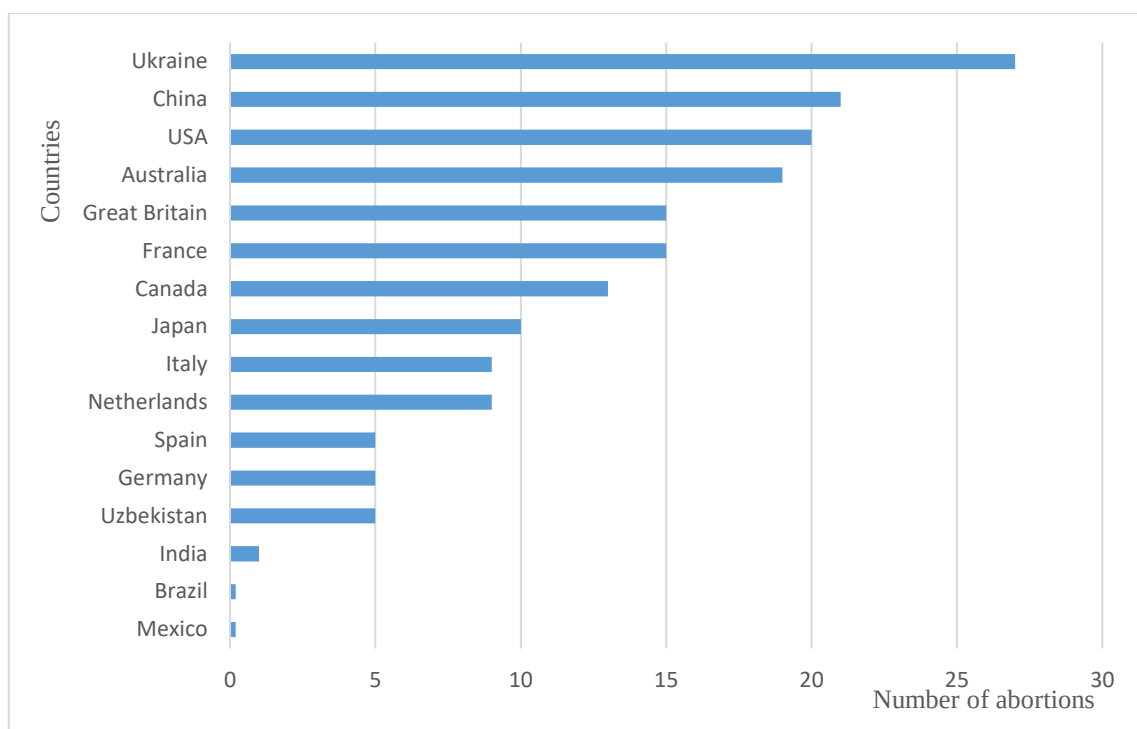


Figure 1. The number of abortions in most countries per 1000 women aged 15 to 44

In the structure of abortions in 2020, 68,6% of women living in cities and 31,4% of women living in villages. This is due to fact that share of urban population is 2/3 of the total population.

Level of abortions by age groups according to results of a sociological study are shown in Fig. 2.

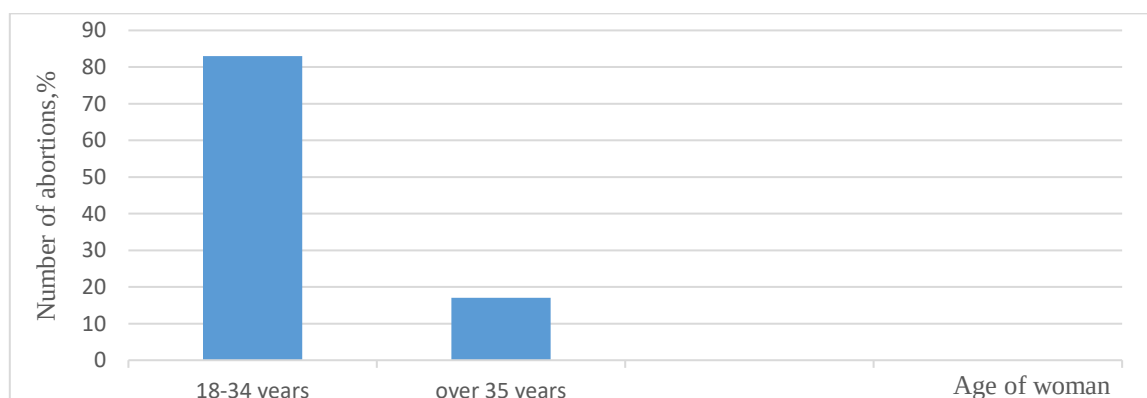


Figure 2. Number of abortions depending on the woman's age

Main reason for abortions, according to experts, is ignorance and unwillingness of Ukrainian women to use modern methods of preventing unwanted pregnancies, including hormonal drugs [181]. An important point in this matter is lack of awareness

of wide choice and possibility of individual selection of effective contraceptives for each woman. It is possible to take into account not only phenotypic and age features, but also to choose a convenient dosage form with a certain mode of application [182, 183].

Recent research have shown that family planning through increased use of spermicides has a beneficial effect on women's health.

In recent years, significant progress has been made in medicine and pharmacy in improving and supplementing arsenal of contraceptives. Schemes have been developed to take into account characteristics of each woman, namely: health status, presence of bad habits, working conditions, individual needs, fertility phase, age etc.

Modern methods of contraception are divided into: physiological, barrier, chemical, hormonal and antihormonal, intrauterine therapeutic systems (ITS), surgical. To assess effectiveness of each method of contraception, Pearl Index is usually used, which shows number of pregnancies in 100 women during the year when using a particular method of contraception. The lower this figure, the greater effectiveness of the method of contraception [184].

Contraceptive methods play an important role in preserving women's reproductive function, as they not only prevent unwanted pregnancies but also reduce risk of sexually transmitted infections. Therefore, choice of a particular method of contraception is important in the prevention of these diseases [185, 186].

The most common method of contraception is oral. We conducted research (pharmacy-based questionnaires) on women's adherence to certain types of contraception and compared it with use of contraceptives by women in Western Europe (based on literature analysis) (Fig. 3).

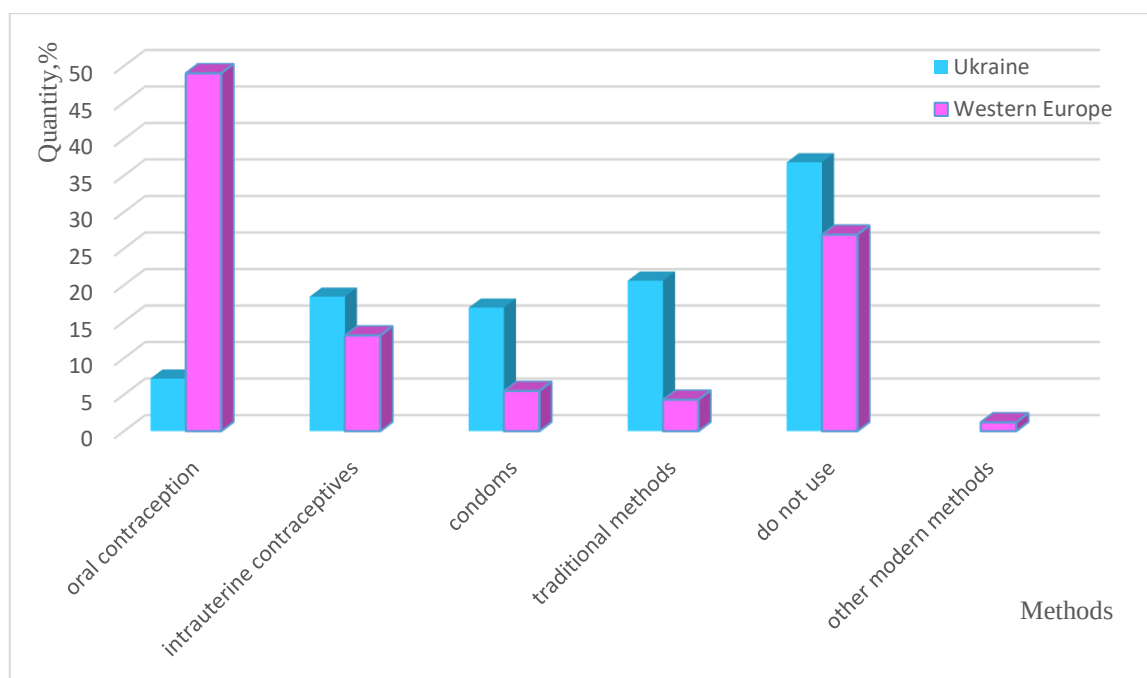


Figure 3. Use of contraceptive methods by women in Ukraine and Western Europe

As can be seen from Fig. 3 significant number of women use oral method of hormonal contraception. However, use of oral contraceptives has a number of side effects: cardiovascular disease, nausea, mood swings and depression, decreased libido and more. The main disadvantage of oral contraceptives is lack of ability to prevent the transmission of sexually transmitted diseases.

Based on the above, it can be argued that the main areas of women's reproductive health are to address two issues: prevention of unwanted pregnancies and medical abortion; prevention of sexually transmitted infections.

At the present stage, the State Pharmacopoeia of Ukraine, as well as pharmacopoeias of leading countries, distinguishes a group of drugs for vaginal use - liquid, soft or solid drugs intended for vaginal administration to ensure local action, namely: pessaries, vaginal tablets and capsules, vaginal solutions, emulsions and suspensions, tablets for preparation of vaginal solutions and suspensions, soft drugs for vaginal use (ointments, creams or gels), vaginal foams and tampons [187].

Topical contraceptives have certain specifics, namely that in order to have a spermicidal effect, local contraceptives (LC's) must have good permeability and meet a number of requirements. Namely: have high adhesion to vaginal tissues, ensure

accurate dosing and stability of the drug concentration, do not show side effects, do not irritate the vaginal mucosa, do not affect the vaginal microflora, do not penetrate into the blood, maintain physicochemical parameters during the shelf life, to be comfortable in application, convenient at transportation and storage.

Using of mild dosage forms (MLD) in gynecological practice has certain features that are associated with the complex relief of the vaginal mucosa and its constant hydration.

Much of the local contraceptives are available mainly in form of suppositories, which, until recently, was considered a universal form and was prescribed to almost all women. However, results of a study of the convenience of using local contraceptives, conducted by specialists of the family planning department of the NSI of POG of the NAMS of Ukraine revealed a feature: for women, the time factor is important. It takes 10 to 15 minutes for the suppositories to take effect, which may be considered inconvenient by some patients.

Intravaginal use of metronidazole has been suggested to prevent vaginal infections. Results of comparative studies have shown the high effectiveness of metronidazole (91%), used in the treatment of bacterial vaginosis (BV) [188].

Oral metronidazole may be complicated by diarrhea, allergic reactions: urticaria, skin rash. Due to the fact that oral administration has a significant number of adverse reactions, many clinicians prefer vaginal route of administration, which is not inferior to the effectiveness of oral therapy. It is best because of the lower likelihood of side effects, as well as the possibility of treating pregnant women and breastfeeding women. Currently widely used metronidazole gel 0,75%, which is used intravaginally. The efficiency of its use is 85 - 91%. The only manufacturer of metronidazole in the form of a gel in Ukraine is Unique Pharmaceutical Laboratories India.

Gels are cohesively dispersed ultra- and microheterogeneous dispersed systems with gaseous and liquid dispersion media, which have some properties of solids, including ability to retain shape, some strength, plasticity, often elasticity.

Gels are formed from highly dispersed systems during their coagulation, when the particles of the dispersed phase due to molecular adhesion (due to molecular forces

of different nature) form a spatial grid, while system does not stratify. Gels are formed due to loose coagulation by a relatively small number of coagulation centers on the surface of particles of dispersed phase. A group of typical gels is formed by lyophilic (reversible) highly dispersed systems of colloidal surfactants. Gels are formed from corresponding sols when concentration of colloidal surfactants increases or when temperature decreases. A specific property of typical coagulation structures is thixotropy — ability of gels to be released spontaneously in time after destruction due to mechanical action, as well as to turn into a sol under action of physicochemical factors. Gels can be not only coagulation-thixotropic, but also condensation-crystallization structures. The latter are formed from typical lyophobic sols, between the particles of which there is a chemical bond. They have high strength and break down without reversible [189]. Gels for contraceptive vaginal use have a number of positive characteristics. They are convenient because they can be used on any day of the cycle, they can be used immediately before sexual intercourse. In addition, barrier contraceptives do not affect a woman's hormonal background, and therefore are ideal for nursing mothers.

Creams are heterogeneous dispersed systems based on emulsions, which have a Newtonian type of flow and low values of rheological parameters. Their widespread use in medical practice is due to possibility of a combination of immiscible liquids, regulation of bioavailability of substances, elimination of irritating effects on skin and mucous membranes of certain substances. There are direct emulsions (type o/w), inverse (type w/o), and multiple, in which drops of the dispersed phase serve as a dispersed medium for smaller drops. Depending on the type of emulsion base, creams, in turn, are divided into hydrophobic (based on emulsions w/o or o/w/o) and hydrophilic (based on emulsions o/w or w/o/w), stabilized by appropriate emulsifiers. Hydrophilic creams also include colloidal dispersed systems consisting of water-dispersed or water-glycol solvents higher fatty alcohols or acids stabilized by hydrophilic surfactants. Type and properties of cream depend on composition, ratio of liquid phases, quantity and chemical nature of emulsifier, method and temperature of manufacture and other factors. Low-concentration emulsion systems are typical liquid

drug systems. As concentration of dispersed phase increases, the viscosity of system increases sharply, system becomes gelatinous and acquires properties of a gel [189].

Vaginal cream has a contraceptive effect immediately after administration and retains its effect for a long period of time.

Use of ointments to affect local processes has been known since ancient times, but for a long time vaginal soft drugs have been positioned mainly as a means of local contraception [190].

In fact, only in the 90's of the twentieth century, due to development of medical and pharmaceutical science, formed an understanding of importance of right choosing not only drugs but also soft dosage form to ensure proper effect of topical therapy, determined by severity of inflammation and desired depth effects: the more acute process, the milder selected dosage form should act [191, 192].

According to V.A. Golovkin and co-authors, hydrophobic ointments are used to a limited extent in local treatment of women's urogenital tract (usually applied only to paravaginal or perianal areas) due to occlusive effect, and therefore contraindicated in acute inflammatory processes [192]. In addition, they do not absorb vaginal secretions and are poorly washed off. Use of hydrophobic ointments, according to some authors, is appropriate for chronic diseases of external genitalia as carriers for antifungal and analgesic drugs.

In the topical treatment of both acute and chronic gynecological diseases can be used emulsion ointments and creams, as well as hydrophilic mild drugs. Because they are easily mixed with vaginal secretions, do not interfere with moisture and gas permeability of the mucous membrane, can adsorb significant amounts of secretions and exudate, and are easily washed off without leaving a greasy mark.

Biopharmaceutical studies conducted during this period have shown that the most effective therapeutic effect is provided in the presence of drugs in a mild dosage form in dissolved state. Taking into account hydrophobic properties of most antibiotics, antimicrobials and antifungals, the main efforts of researchers were focused on development of emulsion ointments and creams for treatment of women's urogenital tract.

Thus, in 1990, Hillier S. and co-authors established feasibility of topical treatment of bacterial vaginosis using clindamycin phosphate as an emulsion cream [193].

A study by a team of researchers led by M. Bourin of the pharmacokinetics of clindamycin phosphate in the form of 2% cream showed the degree of bioavailability of local application of this antibiotic, appropriate to systemic therapy, but with fewer side effects, which allowed to recommend this dosage form for inclusion in standard treatment regimens for infectious processes in the vagina [194].

During same period, drug manufacturers developed vaginal creams with cyclopiroxolamine, clotrimazole, econazole nitrate, ketoconazole, natamycin, estriol, and improved form of vaginal applicators, which replaced dosage with a syringe [195, 196].

In Ukraine during the 90's of the twentieth century, research was focused mainly on development of composition and technology of multicomponent vaginal creams and gels. Thus, V.A. Golovkin substantiated composition and technology of vaginal cream with a substance that has a wide range of antimicrobial action, mebetisol and anti-inflammatory component - sodium salt of mefenamine [197].

Collective of authors led by V.A. Golovkin proposed, for purpose of local therapy of inflammatory diseases of urogenital tract of women, vaginal cream with nitroxoline [197].

In the XXI century, due to the further increase in incidence of infectious and inflammatory diseases of reproductive tract of women and development of resistance to major groups of drugs which have been used for a long time for their treatment, continues study of effectiveness of clinical use of existing drugs. Thus, effectiveness of intravaginal use of metronidazole in the treatment of bacterial vaginosis was proven in randomized placebo-controlled studies conducted in 2002 by Koumans E.N. with co-authors: topical therapy using 0,75% metronidazole gel (5 g once every 5 days) is as effective as oral use (500 mg twice daily for 7 days) [198].

According to A.A. Khryanin and O.V. Reshetnikov, relative bioavailability of 1% vaginal gel metronidazole is in 2 times higher than bioavailability of vaginal tablets

of 500 mg with a single injection, due to the high ability of drugs from gel base penetrate secretion of vaginal mucosa. Randomized comparative and placebo-controlled studies have shown clinical benefits of 7-day vaginal use of 2% clindamycin phosphate cream over oral use of 300 mg clindamycin twice daily for 7 days [199].

Also at the present stage, search for new combinations of active substances and substantiation of the type of dosage form continues in order to more fully influence pathogens that cause development of PID. Thus, E.V. Drogovoz for treatment of nonspecific vaginitis developed a combined cream containing clindamycin and miconazole, which due to combination of two active substances provides a wide range of effects, including anaerobic microflora, with minimal manifestations of systemic side effects [200].

The combination of clindamycin antibiotic with antifungal component terbinafine in vaginal cream on the background of experimental traumatic-bacterial-fungal vaginitis in experimental animals has been pharmacologically reasonable [201].

A group of researchers led by S.S. Kamaeva processed composition and technology a number of vaginal ointments with antimicrobial and contraceptive action, API's of which are ethonium, chlorhexidine bigluconate and sodium sulfacyl [202].

Therewith, it can be stated that the available range of soft vaginal drugs for treatment of infectious and inflammatory processes is limited and does not fully solve the problem of effective treatment of reproductive tract of women.

The development of nanotechnology, as a basic concept of the early XXI century, led to creation of drug pellicle - a fundamentally new dosage form, which belongs to therapeutic systems with controlled release of API and directed their entry into certain organs, tissues or cells [190].

Using pellicle in treatment of gynecological diseases allows to provide topical action in area of pathology or as close as possible to it, while achieving a significant reduction in single and course doses of drugs and, consequently, reducing toxicity, intensity of side effects and violation of natural defense and compensatory mechanisms of organism [190].

Production of pellicle based on polymers provides them with sufficient plasticity to attach to mucous membrane of urogenital tract and long-term retention on it, which favorably distinguishes vaginal pellicle from tablets and capsules. Vaginal pellicle also have an advantage over creams and ointments, as they are able to provide a prolonged effect with a given rate of drug release at site of application [203].

The above has caused considerable interest of leading scientific schools in Ukraine and other countries in the development of this dosage form. According to results of research conducted during last decade, vaginal medicinal pellicle with antibiotics - tetracycline, nystatin, gentamicin, erythromycin, intended for treatment of gynecological diseases have been proposed.

Rudko O.O. developed the composition and technology of medicinal pellicle with ofloxacin for the treatment of infectious diseases of the urogenital tract [204], and Kulish O.I. and co-authors developed medicinal pellicle with prolonged release of cephalosporin antibiotics - cefazolin and cefotaxime [205].

For treatment of inflammatory diseases of the urogenital system of women T.N. Litvinenko processed the composition of 2 polymer pellicle: quinozol, a substance with pronounced antiseptic, antibacterial and antifungal effect [206] and gentamicin sulfate [207].

Possibility of using BAS of medicinal plants to provide anti-inflammatory, antiseptic, antimicrobial and reparative action in treatment of diseases of women reproductive system is being actively studied. Medicinal pellicle with extracts of yarrow, fennel, chamomile, sage, plantain, aloe and with romazulan and chlorophilipt have been proposed [208].

The analysis historical stages of development of the main types DF intended for topical effects on infectious and inflammatory processes of the reproductive tract of women, shows the relevance of inclusion in the treatment process of gynecological nosologies of modern drugs, created taking into account specifics of the penetration of API through the mucous membrane of the female genitalia and able to influence the main elements of etiology and pathogenesis of this group diseases.

Particular attention should be paid to the health of pregnant women and to improving the organization of pharmaceutical supply.

Author Gravchenko L.O. [179] formed a socio-demographic portrait of contraceptive users, determined characteristics of consumer behavior, including motivation and purpose of consumption, calculated coefficients of availability in local pharmaceutical market, which allows specialists of medical institutions and pharmacies to make informed decisions about rational contraception women of different ages, considering gynecological health and economic affordability. A methodological approach is also proposed, which is based on the results of comprehensive research and the concept of improving pharmaceutical care (PC) in the field protection of reproductive health.

Maksimovich N.M. in her scientific works [209] substantiated approaches to improving information support of rational use of drugs during pregnancy according to evidence-based medicine, developed methods of pharmacoeconomic analysis of treatment diseases in pregnant women to optimize cost of pharmaceutical care and reimbursement. She developed medical records of patients (214 documents) from gynecological departments of district and regional hospitals and a specialized center clinical protocols governing treatment of diseases of pregnant women: preeclampsia (PE), threat of premature birth (TPB), nausea and vomiting (NVP); analysis of the range of registered drugs for the treatment of PE, TPB, NVP in accordance with WHO recommendations, British National Form (BNF) in comparison with the State Register of Medicinal Products of Ukraine (SRMP), State Formulary of Ukraine (SF); systematized evidence of efficacy, safety of drugs, including herbal, for rational pharmacotherapy of pregnant women. Author also analyzes incidence and prevalence of diseases during pregnancy in Ukraine and world; treatment standards of international organizations for treatment process [209].

Saltuk O.V. [210] researched question improvement of pharmaceutical care for pregnant women, analyzed key objective and subjective factors, which influencing compliance of pregnant women and created a medical and social portrait of target consumer of PC among pregnant women, estimated cost of medical care for pregnant

women in outpatient settings treatment. Also were calculated costs of pharmaceutical care for pregnant women in provision of inpatient and outpatient care from point of view of distribution of sources of funding for PC, which allows to optimize costs in implementing the strategy of providing PC to pregnant women suffering from pathology.

Author conducted a marketing analysis of range of drugs within of outpatient and specialized medical care, studied individual cards of pregnant women and letters of appointment from history of pregnancy and childbirth, and developed a universal algorithm for drug selection in formation of pharmaceutical counseling.

An analysis of domestic and foreign literature confirms conclusion that most domestic studies conducted by specialists in clinical pharmacology are aimed at the clinical aspect of therapy for pregnant women, with insufficient attention paid to complex problem of organizing medical care for this socially significant category of population.

In scientific publications there are isolated studies of prescriptions for pregnant women, including marketing analysis of range of drugs, pharmacoeconomic analysis of assortment (ABC-, VEN-, frequency analysis, analysis cost of medical care for pregnant women), evaluation of prescriptions in terms of fetal safety; assessment of compliance with pregnant women [210]. However, the practical solution of the problems of scientific and methodological support of PC for pregnant women requires in-depth research on development of the concept of PC for pregnant women with pharmacoeconomic justification of treatment regimens. We have proved that due to the high medical and social importance of pregnant women's health, certain aspects of providing PC to pregnant women (pharmaceutical consulting, safety of fetal medications, etc.) have not been reflected in current concept of PC in Ukraine.

Research of Kasyutina O.L. [211] deserves attention on development of scientifically sound methodological approaches to improve quality of life of pregnant women by optimizing supply of drugs and conditions of their rehabilitation at the regional level. Particular attention is paid to current state of government regulation of social protection of pregnant women and legal framework governing, which regulates

the organization of affordable medical and social care for women during pregnancy and childbirth. Author analyzes features of medical care for pregnant women at stages: outpatient, inpatient and spa treatment, conducted an expert evaluation of the range of drugs intended for treatment and prevention of pregnant women to establish their safety, effectiveness, rationality and frequency of use.

Using factor analysis (Delphi method) [211] identified the main factors that have the highest level of impact on drug consumption during pregnancy, namely: pregnancy complications, infectious diseases and cases of self-medication.

According to FDA classification, [211] was segmented according to safety categories assigned to pregnant women, which confirms the need for regular monitoring of compliance with the principles of "medicalization" and evidence-based medicine selection and appointment of safe drugs for pregnant women. Also noteworthy are algorithm and methodological approaches to building an organizational and functional model based on the principles of "medicalization" of drugs and optimization of assortment policy in system of medical care for women during pregnancy, which will improve quality of life of pregnant women.

Shilkina O.O. [212] conducted research that includes scientific substantiation of methodological approaches to improving the system of pharmaceutical care in Ukraine by developing and elaboration recommendations for establishment of pharmacist protocols and tools to ensure quality in pharmacies in standardization of medical and pharmaceutical care.

In order to integrate into modern domestic health care system, a group of authors [213] proposed a model of the PC process, which involved specialists in practical pharmacy to provide PC on the rational use of contraceptives, and a draft pharmacist's protocol for dispensing over-the-counter medications to prevent unwanted pregnancies and promote family planning [213]. For this purpose the general classification of indicators of quality of PC on signs and properties as a component of medical care was offered, and also features of a choice of a method of their calculation are defined.

Preservation of women's reproductive health is an integral part of Ukraine's demographic policy, so the organization of measures to improve prevention, diagnosis

and treatment of women, pharmaceutical care for the rational use of contraceptives remains an urgent problem that requires more in-depth analysis and regular monitoring of medical principles.