ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Prevention Of Adhesions In The Preservation Of Reproductive Health Of Women With Endometryoid Cysts.

Boychuk AV[1]*, Kurylo OU[2], and Tolokova TI[3].

*[1]MD, PHD, professor of the Department of Obstetrics and Gynecology Ternopil State Medical University
[2]MD, postgraduate student of the Department of Obstetrics and Gynecology Ternopil State Medical University
[3]MD, Ternopil State Medical University, associate professor Department of Medical Bioethics and deontology

ABSTRACT

The article presents of our work is determined by the need for a detailed study of pathological factors, an objective clinical assessment of the status of individual parameters of the ovarian reserve in patients with endometrioidal ovarian cysts and infertility after laparoscopic cystectomy, the development of therapeutic tactics aimed at minimizing complications and relapses of the disease with the use of the biodegradable antiadhesive medical substance Defensal®. In 2005 – 2016 years 186 patients with external genital endometriosis suffering from infertility who underwent planned operative treatment were examined. The main group included 106 patients who underwent planned laparoscopic intervention and antiadhesive mean Defensal®. In the comparison group (80 patients), therapeutic measures were conducted in the traditional volume. The effectiveness of therapy was assessed by the results of dynamic studies of the ovarian reserve, the identification of the adhesion process of the pelvic organs with bimanual examination, ultrasound. Long-term results of treatment were observed in the patency of the fallopian tubes in hysterosalpingography and in the frequency of pregnancy. The reproductive potential in the main group of patients, on the basis of changes in the markers of the ovarian reserve, in correlation with the results of bimanual, ultrasound, hysterosalpingoraphy, was confirmed as complete more reliably than in the comparison group ($p < 0.05$). The authors own research indicates that the use of the drug Defensal® allows to expand the spectrum of possibilities for pathogenetically substantiated treatment of patients with endometriosis and to significantly increase its clinical effectiveness directed primarily at restoring reproductive function in patients of childbearing age.

Keywords: infertility, endometriosis, adhesion, complex treatment, ovarian reserve, Defensal®.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

In modern medicine, the medico-social problem of timely diagnosis and effective treatment of genital endometriosis, which is in one of the first positions in the structure of gynecological morbidity, occupies the central place in the way of preventing violations of the function of the female reproductive system [5]. Recently, there is a clear tendency to rejuvenate this disease. The international association of endometriosis found a fairly early average age of primary manifestation - 15.9 years, which is extremely unfavorable for the prognosis of female fertility [15].

A recent EndoCost study of the World Endometriosis Research Foundation (WERF) found significant costs associated with the management of patients with endometriosis in specialized clinics that have reached an economic burden at least similar to that of other chronic diseases such as sugar diabetes. [14] In addition to economic problems, endometriosis also has a significant impact on various aspects of women's lives, including social and sexual relations, work and study (De Graaf, et al., 2013, Nnoaham, et al., 2011, Simoens, et Al., 2012).

Analysis of research and publications: analizing data publications, it should be note a main goal of gynecological care is to identify patients with a high risk of developing conditions potentially threatening the violation of the realization of the reproductive capabilities of women [2].

One of the most common forms of genital endometriosis is endometriosis of the ovaries [13]. Many researchers noted an increase in the frequency of localization of endometriosis lesions in the ovaries, as well as the direct effect of endometrioid ovarian cysts on the incidence of infertility [4, 11].

The normal ovary does not seem to be an important source of cancer antigen or carbohydrate antigen 125 production [20]. However primary cultures of human ovarian surface epithelial cells secret detectable but lowest concentration of CA-125. A number of benign conditions can cause elevations of the CA-125 level, including endometriosis, uterine fibroids (benign tumors), normal menstruation, pelvic inflammatory disease [19, 22].

To maintain the reproductive function in this pathology, it is necessary to take into account changes in the ovarian reserve. According to the researchers, the ovarian reserve refers to the reproductive potential of each oocyte and that part of the pool of primordial follicles, which remains at the concurrent point in time when the ovaries are affected by endometriosis [10].

Antimullerian hormone (AMH), also known as a Muller inhibitory substance, is a dimeric glycoprotein that belongs to the family of transforming growth factors beta. In women from the moment of birth and before the onset of menopause, AMH is produced by granulosa cells of growing folicles in the ovaries. The concentration of AMH in women correlates with the number of antral follicles and best reflects the decline in reproductive function in healthy women with proven fertility, and is also a necessary test in a comprehensive assessment of the ovarian reserve [16].

The level of AMH remains relatively constant throughout the menstrual cycle, reflects the continuous, unrelated growth pattern of young follicles in the menstrual cycle, which makes the determination of the concentration of this hormone a primary informative marker for inhibiting the selection of primordial follicles and a decrease in the effectiveness of foliculogenesis stimulation with follicle-stimulating hormone [1]. The level of serum follicle-stimulating hormone (FSH) has traditionally been used as a marker of ovarian reserve, but it is limited by large cycle-to-cycle variation, requiring repetitive measurements to be applied clinically. In some cases, it is not as powerful as the genital endometriosis, but can be used to diagnose of ovarian reserve together with other markers [21].

The main areas of treatment for genital endometriosis include surgical, hormonal and combined. The surgical approach, with inevitable invasiveness, must necessarily ensure a reduction in the risk of relapse and the preservation of the woman's genital function. Laparoscopy allows direct surgical treatment and the stage of the disease, which can be performed using the ASRM classification system (classification of the endometriosis of the American Society of Reproductive Medicine in the latest version of 1996, 1997), which does not properly reflect the intensity of the pain syndrome accompanying endometriosis and infertility. Any

surgical intervention is accompanied by tissue necrosis in the focus of inflammation, pathological protein catabolism, mass death of cells and the development of toxic states, which leads to neurovascular changes in the ovaries, a decrease in the ovarian reserve and generative possibilities. [8, 17].

In this regard, the request for medical assistance is the development of clear guidelines for the diagnosis, therapy and rehabilitation of this category of women. Imbalance and delay of medical measures can lead to the development of complications, namely the emergence of postoperative adhesions. The formation of the adhesive process is the reaction of the peritoneum to trauma. With a certain localization, prevalence and severity of adhesions, a peritoneal edema disease is formed. Peritoneal adhesions of varying severity can occur in 93-100% of patients who underwent abdominal surgery. According to various data, in 20-40% the adhesions formed after surgical intervention disrupt the quality of life of patients and often are the causes of intestinal obstruction, the occurrence of acute and chronic abdominal and pelvic pain, dyspareunia [7, 9, 12].

In scientific research, the search for new opportunities in the prevention and treatment of peritoneal adhesions does not stop. These issues are of special importance in connection with the causal relationship of surgical interventions and tubal peritoneal infertility. [3, 6]

Postoperative adhesions reduce the degree of satisfaction of patients' vital needs and are the cause of difficulty during repeated surgical approaches, prolong the duration of surgery, increase the risk of iatrogenic internal injuries in repeated operations, intestinal obstruction, chronic pelvic pain [18].

The purpose of our work is determined by the need for a detailed study of pathological factors, an objective clinical assessment of the status of individual parameters of the ovarian reserve in patients with endometrial ovarian cysts after laparoscopic cystectomy, the development of therapeutic tactics aimed at minimizing complications and relapses of the disease.

The aim of our study: investigate pathological factors, an objective clinical assessment of the status of individual parameters of the ovarian reserve in patients with endometrioid ovarian cysts and infertility after laparoscopic cystectomy, development of therapeutic tactics aimed at minimizing complications and relapses of the disease with the use of the biodegradable antiadhesive substance Defensal®.

MATERIALS AND METHODS

Under our supervision there were 186 patients who were examined and treated at the gynecological department of the Ternopil municipal hospital No 2 from 2005 till 2016 years for external genital endometriosis. The duration of the disease was (8.6 ± 0.7) years. The age of the patients ranged from 22 to 32 years. Patients were divided into two groups homogeneous according to anthropometry, gynecological, reproductive, somatic, infectious anamnesis, with unilateral and bilateral endometriosis, ovarian formations, depending on the complex therapeutic approach.

Primary infertility was in 132 (71.0%) women, secondary infertility in 29.0% (54 patients).

Patients enrolled in the study included a thorough history survey: the age of the menarche, the characterization of the menstrual cycle, previous pregnancies and their results, the use of hormonal therapy, a surgical and family history, regarding endometriosis or malignant gynecological neoplasm.

All patients underwent gynecological examination, including vaginal examination using mirrors, as well as bimanual and rectovaginal palpation. For the objectification of the changes revealed during gynecological examination, the methods of transvaginal ultrasound were used, if necessary, magnetic resonance imaging, cystoscopy in the presence of appropriate complaints. Patients with the main symptoms of endometriosis were allocated to the observation group: pain syndrome, dyspareunia, dysuria, psychoneurological disorders, reproductive disorders (infertility and miscarriage).

The analysis of anamnestic data, clinical and laboratory examination, gynecological examination, ultrasound, determined the level of CA 125, AMH, FSH.

All the patients examined at the first stage underwent operative endoscopic intervention "First-look" with observance of the principles of reconstructive-plastic conservative surgery with the informed consent of

the patient for possible expansion of the scope of the operation, if necessary. We used the method of extracting the endometrioid cyst within a healthy tissue with minimal coagulation along the wound. The ovarian reserve of patients based on the results of the triple test (CA 125, AMG, FSH) was compared with the expected reserve for women of this age, which allowed controlling the expected reproductive capacity. Hormonal studies were performed on the 2-3rd day of the menstrual cycle, 3 and 6 months after the surgery.

When approaching the choice of the scope of intervention, preference was given to organ-preserving capabilities, which is extremely important for patients of reproductive age who are interested in preserving the genital function. Laparoscopy was performed using endoscopic equipment with a tool kit according to the generally accepted procedure. With an overview laparoscopy, the endometrioid heterotopia values were estimated, their number, maturity determined by color and shape, the presence of endometrioid cysts and adhesions.

We used the method of enucleation of cysts within a healthy tissue with minimal coagulation along the wound. Surgical treatment of endometriosis was aimed at maximum removal of endometrioid heterotopies - ovarian cysts, implants on the peritoneum with the purpose of restoring normal, anatomical relationships of the pelvic organs. Electrocoagulation of individual endometriotic foci was carried out using monopolar and bipolar electrodes. Small (less than 2 cm) endometriomas were cut, the contents evacuated, the shell of the tumor-shaped formation was carefully lapped and / or its bed was coagulated. In 106 cases (group 1), after completion of surgical manipulations and restoring the integrity of the anterior abdominal wall through tubular drainage, an intraperitoneal injection of the antifungal drug Defensal® was carried out 50 ml once after operation, 80 women who underwent traditional abdominal irrigation with a normal physiological solution entered the second group

Dynamic monitoring of the effectiveness of the prescribed therapy was performed: ultrasound (1 time per 3 months) and determination of the level of CA 125 tumor markers in the blood serum for the purpose of early diagnosis of recurrence of endometriosis. The degree of patency of the fallopian tubes was assessed by intraoperative chromosalpingoscopy and after 1.5 - 2.0 months when hysterosalpingography was performed according to a conventional method using iodine-containing contrast agents.

Statistical processing was carried out on a personal computer using a statistical software package, namely using Student's test (t). The difference between the comparative averages was considered probable at $p < 0.05$.

All patients underwent laparoscopic cystectomy. The control group (n = 30) consisted of conditionally healthy women of similar age who had no history of operative ovarian interventions, who underwent a clinical and laboratory examination, ultrasound to confirm the state of health.

RESULTS OF THE RESEARCH AND THEIR DISCUSSION

The recurrent course of ovarian cysts was diagnosed in 56 (30.1%) patients, 20 of them had surgical treatment in anamnesis, in 35.7% of cases, ovarian resection was performed, and 64.3% had cystectomy.

Analysis of clinical and anamnestic data showed that the main complaints in patients with endometriosis were chronic pelvic pain that worsened before menstruation in 65.1% with genital endometriosis and 12.0% in the control group, dyspareunia in 61.6% Patients of the main group and 8.0% in the group of healthy women. These symptoms of the disease most often combined in different combinations and met with the same frequency in women with external genital endometriosis at different degrees of damage. By the objectivization of the intensity of painful manifestations - from moderate to intolerant - on a 10-point scale 0 corresponded to complete absence of pain, and 10 - pain of intolerable intensity, severe pain was diagnosed in all women with grade III manifestations of endometriosis, mainly dysmenorrhea and dyspareunia, but insignificant Moderate (3-5 points) - with I and II degrees, in most cases - prolonged non-cyclic abdominal and pelvic pains, lower abdominal pain and lower back.

Primary infertility was observed in 71.8% of the examined, secondary infertility 28.2%.

The performed transvaginal ultrasound studies revealed the following most characteristic signs of the first degree of prevalence of genital edometriosis: small (up to 1 mm in diameter) anechoic tubular structures, directed from the endometrium to the myometrium in 65% of cases; Appearance in the basal layer of the endometrium of small hypo-and anechogenic inclusions of the round and ovoid form with a diameter of about 1-2 mm in 67 women; The irregularity of the thickness of the basal layer of the endometrium and the serration or ruggedness of the basal layer of the endometrium was detected in 48%; Detection of local endometrial defects in 18%; Appearance in the myometrium, intimately adjacent to the uterine cavity, areas of increased echogenicity up to 3 mm thick. In 46 patients with grade I endometriosis, the thickness of the uterine walls by ultrasonic characteristics was close to normal. An increase in the thickness of the walls of the uterus, exceeding the upper limit of the norm on ultrasonography, was revealed in 51 patients with grade II endometriosis. Occurrence in the zone of increased echogenicity of small, round anechogenic formations with a diameter of 2-5 mm, as well as fluid cavities of various shapes and sizes containing finely dispersed suspension (blood) and sometimes dense inclusions of small echogenicity (blood clots) was diagnosed in 53%. Ultrasound signs of grade III prevalence of genital endometriosis, manifested by an increase in the uterus in the anteroposterior size of 85%; Appearance in the myometrium of a zone of increased heterogeneous echogenicity occupying more than half the thickness of the uterine wall - in 28 patients, detection of anechogenous inclusions with a diameter of 2-6 mm in the echogenic zone, liquid cavities of various shapes and sizes containing finely dispersed suspension was diagnosed in 18%.

Ultrasound criteria coincided with intraoperative diagnosis in genital endometriosis of I degree of prevalence in 88.5% of cases, degree II in 90%, and grade III in 96.2% of cases.

According to the revised classification of the American Fertility Society, which is the international standard for assessing spontaneous evolution and comparing therapeutic outcomes according to the protocol of the Ministry of Health of Ukraine No. 319. It is based on counting the number of heterotopy expressed in points: stage I (minimal changes) - 1-5 points; Stage was found in 46 women, II (minor changes) - 6-15 points; The stage was detected in 80 patients; III (expressed changes) - 16-40 points; The stage was diagnosed in 56 clinical situations, IV (very pronounced changes) - more than 40 points were observed in 4 patients. The presence of 1-5 foci was attributed to a mild form; 6-5 - to moderate; 16-30 - to the heavy; More than 30 foci of endometriosis testified to widespread endometriosis.

Small forms of endometriosis with laparoscopy were manifested in the form of "pupils" that rose above the surface of the peritoneum and had a red, brown, black or green color in 43.0% - 80 patients. In 14.0%, 26 patients had multiple heterotopies in the bladder area.

When laparoscopy was taken into account both the size of the heterotopy of endometriosis, and the degree of the adhesion process. Of all the cases of endometriosis, which we detected with laparoscopy, 79.1% of the patients confirmed the previously diagnosed diagnosis, and in 20.9%, the diagnosis was first established. Often, endometriosis (43.9%), endometriosis of the fallopian tubes and small forms of endometriosis (23.4%) were more common. Retrocervical endometriosis was found in 14.0% of patients. In other cases, there was endometriosis of the uterine ligaments and the vesicle-uterine peritoneum. In 64.5% (120 women) of cases, an adhesive process of varying severity was diagnosed.

Disconnection of the adhesion process during the surgical intervention was most carefully conducted to all patients, with intraoperative indications for this stage of the operation.

Dynamic ultrasound studies for postoperative follow-up showed that surgical intervention using traditional abdominal sanitation with normal saline prevented the formation of parovarial adhesions and ovarian fixation in 56.2% of cases, and the use of an antiadhesions barrier, the drug Defensal®, which, except flotation activity, contains hyaluronic acid - a natural biodegradable component of the extracellular matrix in combination with sparing operational techniques produced good results in 83.6% of cases.

In 13 (16.25%) patients of the second group who underwent laparotomy, violations of permeability of the fallopian tubes due to peritubar accretions were revealed, 42.9% of them had bilateral occlusion or occlusions of one tube. In the 1 group, the violation of patency of the fallopian tubes due to the adhesive process was recorded in 11 (10.4%) people, and bilateral occlusion in 2 (1.86%). Infringement of passableness

of fallopian tubes after laparoscopic operations was revealed in 11 (10.3%) patients of the group receiving in the complex approach the against adhesive drug Defensal®.

In all patients with surgical interventions on the ovaries in history, the level of AMH was at the lower limit of the norm or was significantly lower than normal, averaging 2.5 ± 0.5 ng / ml (normal concentration of AMH 3.0-5.0 ng / Ml, p = 0.025). A re-examination of the hormonal status was performed in 160 (86%) patients. Changes in the content of anti-mullerian hormone were detected - by 12% (in 134 patients) as compared to their indices before surgery.

Table 1 Ovarian reserve of patients with external endometriosis

Indicators	Control Group (n=30)	Before treatment (n=186)	1 group after treatment (n=106)	2 group after treatment (n=80)
AMH	3.91±0,20 ng/ml	1.11±0.22 ng/ml	2.20±0.25* ng/ml	1.3±0.6*,** ng/ml
FSH	8.71±1.09 IU/L	4.2±1.80 IU/L	7.76±0.28 IU/L	5.20±0.80 IU/L*,**
CA-125	26± 6.3 U/ml	48.2 ± 6.3 U/ml	27.2± 6.3 U/ml	35.2 ± 2.3 U/ml*,**

Notes: 1. * - the reliability of the differences between the indicators of the control group and the first group.
2. ** - reliability of differences between the indicators of the first and second groups.

Hormonal studies were performed on the 2-3rd day of the menstrual cycle or on the 2nd-3rd day of menstrual reactions after cystectomy. The average value of FSH concentration in patients with endometrioid ovarian cysts significantly differed from the control group, amounting to 4.2 ± 1.80 IU/L. At the same time, in 17.2%, in 32 women, there was an increase in FSH level of 8-16 IU / L (concentration reaches 9.6 ± 1.8 IU / L), which, according to the literature, is an early marker of ovarian reserve reduction and It is possible to attribute first of all these patients to the risk group of premature ovarian failure. When studying the oncoprotein CA-125 for the timely diagnosis of operable ovarian neoplasm, the degree of inferiority of biological barriers for the penetration of high molecular weight glycoprotein derivatives of coelomic epithelium was determined due to the destructive effect of endometriosis. In the dynamic observation, the repair of barrier mechanisms was diagnosed with the use in a complex approach of surgical treatment of bioavailable substances with high regenerative flotation properties ($p < 0.05$), which is proved by a significant decrease in the CA-125 content in the blood on average to 27,2 U/ml and allows you to judge the productive relationship with a positive perspective on fertility. Our study concludes result specificity of CA-125 agrees with some studies which focused mainly on the validity of serum CA-125 in detection of endometriosis and concluded that it could be used as an adjuvant together with other markers such as anti-mullerian hormone, follicle-stimulating hormone.

All operations of patients were making in the volume of cystectomy. In addition to cystectomy, was also eliminated adhesion (42.8%), endocoagulation of endometriosis (21.4%), myomectomy (10.7%).

The full value of against adhesive effect of the Defensal® was evaluated according to the results of bimanual examination before discharge from the hospital. In vaginal examination, signs of the adhesion process, namely, displacement of the pelvic organs and / or restriction of their mobility, were found in 29 (15.6%) of the first group and in 69 (36.1%) - second groups.

Violation of patency of the fallopian tubes after laparoscopic operations was revealed in 10 (12.5%) patients of the 2 group and in 4 (3.8%) - the 1 group.

Table 2. Assessment of patency of the fallopian tubes

Indicators	1 group (n=106)		2 group (n=80)	
	quantity	%	quantity	%
Passage of the fallopian tubes	85	80,2	35	43.7*
External adhesion process	14	13,2	33	41.3*
Tubal obstruction	4	3.8	10	12.5*

Obliteration of Fallopian tubes	3	2.8	2	2.5
Total	106	100	80	100

Note: * - highly significant p <0.05

Free patency of the fallopian tubes was maintained, according to chromohydrotubes, in 80.2% of the patients of the first group, obliteration of one or both fallopian tubes was diagnosed in 3 patients in the isthmic or interstitial compartment, the external adhesion process in 13.2% in the first group, which is two times less than in the second group (27.5%). Infringement of passableness of one or both fallopian tubes are found out in 3 patients of the first group.

Post-surgical treatment all patients tolerated satisfactorily.

In the dynamic observation of long-term results, 48 (45.3%) women of the first group realized reproductive plans, which is 25.3% higher than the desired results in the second group (16 women). In patients with a history of ovarian resection and cystectomy within 1 year of observation, pregnancy did not occur.

CONCLUSIONS

1. The condition of the ovarian reserve in endometrioid cysts of the ovaries depends to a large extent on the volume and frequency of the surgical intervention. The results of hormonal studies suggest that the most sensitive to intraoperative damage and an indicative marker of the ovarian reserve is antimullerian hormone in combination with the determination of the content of serum CA-125, concentration of follicle-stimulating hormone were significantly higher in endometriosis patients than in control group, and their levels were very useful in predicting the severity of the disease.

2. The results of the performed surgical intervention in a sparing amount allow to predict the restoration of fertility after surgical treatment with the maximum preservation of healthy tissue, which allows to preserve the reserve of ovaries and reproductive health of a woman.

3. Given the importance of improving the socio-demographic situation and preserving the reproductive health of young people, with the further improvement of diagnostic methods, in the treatment of endometriosis it is necessary to use a comprehensive approach to treatment. Based on the analysis of clinical data, it was confirmed that patients who underwent surgical treatment of genital endometriosis have a number of factors that lead to the development of adhesive process, their effective overcoming is possible with the use of an bioabsiorption antiadhesive drug Defensal®, which contributes to the improvement of immediate and long-term results of treatment.

Prospects for further research are to the subsequent study and improvement of antiadhesive barriers in the treatment of endometriosis will make it possible to prevent relapses of adhesions and predict fertility of women due to the persistent effect on the ovarian reserve.

REFERNECES

[1] Adamovska T.N. Evaluation of ovarian reserve by determining the level of secretion of the hormone / T.N. Adamovska // Actual issues of pediatrics, obstetrics and gynecology. – 2012. - № 1 - p. 89-90.
[2] Adamyan L.V., Andreeva E.N., Apolikhina I.A. Endometriosis: diagnosis, treatment and rehabilitation // Federal clinical guidelines for managing patients - Moscow, 2013. - p. 65
[3] Gladchuk I.Z. Prevention of adhesions after surgery nfertile women with uterine myoma and endometriozom / I.Z. Gladchuk, N.N. Rozhkovskaya, A.P. Rogachev and others. // Reproductive Health of women - 2008. - № 5. – p. 148-150
[4] Durasova E.N. Clinical and morphological variants and molecular features of ovarian endometriosis: Dis .... Cand. med. - St. Petersburg, 2011. - 153 p.
[5] Ishchenko A.I., Kudrin E.A. Endometriosis: Diagnosis and Treatment - M.: GEOTAR-MED, 2002. – 104 p.
[6] Kornatsky A.G. Modern possibilities of prevention of intraoperative complications in interventions on pelvic organs / A.G. Kornatsky, G.V. Chubey, N.V. Brazhuk, V.K. Kondratiuk // Clinical Surgery. - 2014. -

№ 6. - p. 62-65.
[7] Lazarenko V.A. First use against biodegradable polymer means "Mezogel" in acute appendicitis / V.A. Lazarenko, B.S. Sukovatykh, A.I. Bezhin et al. // Man and his health. - 2011. - number 1 - p. 51-55.
[8] Matveeva, N.V. Influence endosurgical coagulating effect on ovarian reserve / N.V. Matveeva, AE Ter-Hovakimyan // Doktor.Ru. - 2013. - № 1 (79). – p. 18-20.
[9] Mehtihanov Z.S. Preventing the formation of abdominal adhesions after laparoscopic surgery and gynecological operations // endovideosurgery in a general hospital: Proceedings of the International scientific-practical conference / Ed. E.K. Gumanenko. - St. Petersburg: Human health, 2014. - p. 71-75.
[10] Nazarenko T.A. Meaning of evaluation ovarian reserve in the treatment of infertility in women of advanced reproductive age // T.A. Nazarenko, M.G. Mishiev N.G., N.G. Fanchenko // Problems of reproduction. – 2005. - number 2 - p. 56-59.
[11] Order of the Ministry of Health of Ukraine 06.04.2016 number 319 unified clinical protocols of primary, secondary (specialized) and tertiary (highly specialized) medical care. Clinical management of patients with endometriosis.
[12] A.V. Pyptyuk Integrated treatment of adhesive peritoneal disease using the drug "Defensal" (first experience) / O. Pyptyuk, SB Telemuha, ON Malyutin, LB Telemuha Ukraine // Surgery. - 2015. - № 1. - p. 68-72.
[13] I.S. Sidorova. Features of therapy of endometrioid cysts of the ovaries / IS. Sidorova, A.L. Hunanyan // Obstetrics, gynecology and reproduction. - 2011. - T. 5, №1. - p. 29-32.
[14] Clinical management of patients with endometriosis. Adapted clinical guidelines based on evidence. // State Expert Center of the Ministry of Health of Ukraine – 2016. - 118 p.
[15] American Fertility Society Revised American Fertility Society Classification of Endometriosis // Fertil. Steril. – 1985. – Vol. 43 – p. 347-350.
[16] Anderson R.A. Measuring anti-Mullerian hormon for the assessment of ovarian rezerv: When and for whom is it indicated? / R.A. Anderson, S.M. Nelson, W.H. Wallance // Maturitas. – 2012. – Vol. 71(1) – p. 28-33.
[17] Anti-Müllerian hormone: an ovarian reserve marker in primary ovarian insufficiency / Visser J. A., Schipper I., Laven J. S. E. [et al.] // Nat. Rev. Endocrinol. — 2012. — Vol. 8, N 6. — p. 331-341.
[18] Brochhausen C. Current strategies and future perspectives for intraperitoneal adhesion prention / C. Brochhausen, V.H. Schmitt, D. Hollemann et. al. // J. Gastrointest. Surg. – 2012. – Vol. 16. – p. 1256-1274.
[19] Hussain and Fazal.(2009). Gynecologic tumor markers. New England journal Medicine. 13: 110-30.
[20] Locker GY.,Hamilton S. and Harris M.et al.(2006). Use of tumor markers in endometriosis disease. Journal of Clinical Oncology. 24: 5313-5327.
[21] Sun Mie Kim Anti-müllerian hormone, follicle-stimulating hormone, antral follicle count, and clinical findings as predictive markers of menopause in late reproductive-aged women / Sun Mie Kim, Seok Hyun Kim, Jung Ryeol Lee, Byung Chul Jee, Chang Suk Suh, Joong Yeup Lee,, Ki Chul Kim, Do Yeong Hwang, Jung Gu Kim, Shin Yong Moon // Korean J Obstet Gynecol 2012;55(2):89-97
[22] Tharwa H. Hassan AL-Tai CA19-9 versus CA-125 in Endometriosis / Tharwa H. Hassan AL-Tai, Hayfaa S. AL-Hadithi, Hind S. Abdulsalam // IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). – 2014. Vol. 13, p. 27-30