



THE EFFECTIVENESS OF ULTRASOUND IN THE PRE-GRAVID PREPARATION OF PATIENTS WITH INFLAMMATORY DISEASES OF THE FEMALE GENITAL ORGANS

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Article history:	Abstract:
Received: October 8 th 2021 Accepted: November 8 th 2021 Published: December 14 th 2021	The article provides recommendations for the pre-gravid preparation of patients with inflammatory diseases of the female genital organs and their consequences in infertility and miscarriage. The indications, examination methods in order to clarify the genesis of the inflammatory disease and the principles of therapy are set out on the basis of clinical recommendations of 2012. The effectiveness of a broad-spectrum antibacterial drug amoxicillin / clavulanate in the program of preparing for pregnancy in patients with inflammatory diseases of the pelvic organs is noted, given the significant increase in the incidence of bacterial infection. flora.

Keywords: Ultrasound diagnostics, pre-gravid preparation, urinary tract infection.

Currently, much attention is paid to the issues of planned preparation of married couples for pregnancy and childbirth. According to the literature, more than 40% of pregnancies are unplanned and, given the high incidence of undiagnosed pelvic inflammatory disease (PID), end in spontaneous abortion, premature birth, intrauterine infection of the fetus and postpartum complications [1, 2]. Every 3-4th married couple turns to foreign gynecological clinics in order to prepare for the expected pregnancy. The number of married couples solving similar problems in our country is much lower, which is due to the lack of knowledge about pre-conception training programs both among obstetricians and gynecologists and among female patients. [3, 4].

In recent years, a clear dependence of the health of the offspring on the age of the parents, indicators of their health, heredity, educational level, material and marital status has been established. The results of one of the studies showed that in the control group, where the children were born were healthy, the parents were in a registered marriage, this pregnancy was desired and planned. In the group of children with moderate perinatal risk, there was a significant influence of such negative factors as aggravated obstetric and gynecological history and the presence of 5-6 damaging factors at the same time, which is the reason for the threat of termination of pregnancy, preeclampsia, placental insufficiency and other complications. In the group of children with a high perinatal risk, the leading negative factors were the age of the parents (over 35-45 years old) and the burdened somatic and gynecological history [3].

Preconceptional preparation includes a set of activities aimed at preparing a woman and her spouse for pregnancy. It is known that the effectiveness of measures to protect the health of mothers and children and the prevention of various complications is most noticeable if they are started before pregnancy [5]. The health of the father is as important as that of the mother in the birth of healthy offspring. In addition, the health of the unborn child depends not only on the health of both spouses, but also on social, psychological and economic conditions.

Participation in the examination before the planned pregnancy of both spouses is also associated with a high incidence of PID, a significant part of which for long-time proceeds without pronounced clinical symptoms. Chronic inflammatory diseases of the genitals are mainly detected during examination of patients before a planned pregnancy, after a spontaneous abortion or premature birth, as well as in spouses who are in a sterile marriage.

PRECONCEPTION TRAINING PROGRAMS

Pre-conception preparation is recommended for women planning pregnancy, with and without complaints; patients with infertility; if there is a history of miscarriage. The set of measures aimed at preparing a woman for pregnancy includes taking anamnesis, clinical and laboratory examination in order to identify extragenital and gynecological diseases, as well as complex treatment, if necessary..

Hereditary or extragenital diseases, tuberculosis, endocrine diseases (diabetes mellitus, metabolic syndrome, thyroid diseases), as well as surgical



interventions on the genitourinary organs, revealed when contacting specialists, require consultation with specialists of the relevant profile, in particular, geneticists, therapists, endocrinologists, surgeons or urologists-andrologists.

The incidence of somatic diseases during pregnancy is 12-14%. On the one hand, pregnancy can cause a complication of an existing disease, on the other hand, a number of chronic diseases of a woman can adversely affect the health of the unborn child. Diseases of the perinatal risk include: cardiovascular pathology (congenital and acquired heart defects and hypertension), diseases of the urinary tract, endocrinopathy, diseases of the hematopoietic system, liver, lungs, diseases of the connective tissue, hemostasis disorders, acute and chronic infections, diseases of the nervous system [6].

Thus, the survey program includes [7]:

- identification of hereditary pathology in spouses and, if necessary, consultation of a geneticist;
- clarification of the presence of extragenital diseases (consultation and treatment with specialized specialists);
- examination for urogenital infections (infection screening and treatment);
- tests for TORCH-complex (Toxoplasmosis - toxoplasmosis, Others - other infections, Rubella - rubella, Cytomegalovirus - cytomegalovirus infection, Herpes simplex virus - herpes simplex virus). The determination of IgG and IgM antibodies to rubella, toxoplasmosis, cytomegalovirus and herpes simplex virus types 1 and 2 is carried out;
- hormonal examination - in case of menstrual irregularities, as well as in patients with infertility or miscarriage after excluding the organic causes of these disorders (table);
- examination for congenital thrombophilic diseases - in women with miscarriage;
- endoscopic examination (laparoscopy and / or hysteroscopy with endometrial biopsy) is indicated for all women with infertility and, if indicated, for miscarriage.

DIAGNOSTICS AND TREATMENT OF INFLAMMATORY DISEASES OF THE PELVIC ORGANS

Joint counseling of both spouses allows you to obtain the most complete information about inflammatory diseases of the genitourinary system before marriage and during the period of married life. In patients with infertility and miscarriage, the consequences of PID are most often revealed: impaired patency of the fallopian tubes, adhesions in

the small pelvis, tubo-ovarian formations, chronic endometritis. Among patients with infertility, despite repeated courses of anti-inflammatory therapy, a comprehensive examination practically in 25-30% of cases reveals chlamydia, ureaplasmosis, mycoplasmosis, bacterial infections, candidiasis [1, 7].

A feature of inflammatory diseases of the genitals in recent years is a change in the etiological structure of PID. So, in 52% of cases, associations are found that include 3–7 microorganisms. Recently, obstetricians-gynecologists overestimate the importance of sexually transmitted infections (STIs) in the development of PID, forgetting about the role of opportunistic, aerobic and anaerobic flora. It is known that normally conditionally pathogenic flora is in the body in small quantities, without causing inflammatory diseases of the genitals, and only under certain conditions becomes truly pathogenic [4, 8].

In particular, conditionally pathogenic microorganisms include *E. coli*, staphylococci, streptococci, candida, etc.

Mixed infections caused by several pathogens account for 20-30% in the structure of PID, and in such situations the clinical manifestations of the disease can be absolutely atypical, depending on the characteristics of the interaction between different types of pathogens. With a mixed infection and a chronic course of the process, the frequency of relapses of the disease increases several times [8, 9].

Almost 80% of women with vulvovaginitis, cervicitis, urethritis have a mixed bacterial-fungal-viral infection. The combination of chlamydia and anaerobic flora is diagnosed in 14-24% of cases, chlamydia and trichomoniasis - in 5-10%. Mycoplasma in the form of mono-infection occurs in 12-18% of cases, the frequency of mycoplasmosis increases several times in combination with other microbial agents. In the structure of the bacterial flora in women with PID, enterobacteria are detected in 18.7% of cases, streptococci in 16.6%, corynebacteria in 10%, and obligate anaerobes in 6%. In recent years, the frequency of gonococcal infection has sharply decreased (5.5%) and the frequency of dysbiotic disorders of the vaginal flora has increased (72.8%) [4, 10].

In 25% of women, the acute inflammatory process, despite the timely started treatment, passes into the chronic stage, and chronic salpingitis, oophoritis and endometritis occupy a leading place in the structure of gynecological diseases. Among the causes of female infertility, the consequences of inflammatory processes in the genitals take the first place, and in case of miscarriage - the second [8, 10].



Along with an increase in the incidence of PID and an increase in self-medication cases, the development of drug resistance to most antibiotics is noted. A number of multicenter studies have shown that the increasingly emerging drug resistance is the most difficult in the treatment of patients with various infectious processes, especially of mixed etiology [9].

Considering all of the above, women with a history of inflammatory diseases of the genitals, patients with infertility and miscarriage must undergo a comprehensive examination for urogenital infections. The rules for obtaining clinical material for laboratory research are as follows [1,2].

1. Compliance with the timing of the collection of material, taking into account the ongoing drug therapy with antibacterial, antimycotic and other drugs:

- not earlier than 14 days after the end of therapy to identify pathogens by the culture method or by the method of RNA amplification;
- not earlier than after 4 weeks when using DNA amplification methods (polymerase chain reaction (PCR), real-time PCR).

2. Obtaining clinical material from the cervical canal or vagina outside of menstruation.

3. Conducting various methods of provocation in order to improve the efficiency of diagnostics of urogenital infections is impractical.

Infection screening for patients with PID, infertility and miscarriage includes:

- smear on the degree of purity from the urethra, cervical canal and vagina;
- a smear from the cervical canal to determine by PCR the presence of: *Chlamydia trachomatis*, *Mycoplasma genitalium*, *Trichomonas vaginalis*, *Neisseria gonorrhoeae*, *Candida* spp., *Gardnerella vaginalis*, herpes simplex virus types 1 and 2, cytomegalovirus and human papillomavirus;
- culture study for *Ureaplasma* spp. and *Mycoplasma hominis*;
- bacteriological culture from the cervical canal to determine microflora and its sensitivity to antibiotics (qualitative and quantitative analysis of microflora).

The examination of the spouses should be carried out in the same laboratory, using the same diagnostic test systems, observing the rules for obtaining and storing clinical material for laboratory research [1,6].

Pathogenetically based therapy should be prescribed simultaneously to both spouses by a gynecologist and an andrologist, followed by monitoring the results of treatment.

Standard treatment regimens, according to the clinical recommendations of domestic authors (2012),

are prescribed when a viral infection, *Chlamydia trachomatis*, *Mycoplasma genitalium*, bacterial vaginosis, *Trichomonas vaginalis* is detected based on the results of PCR diagnostics. Antibiotic therapy for the eradication of *Mycoplasma hominis* and / or *Ureaplasma* spp. it is prescribed when the amount of microbial agents is $> 10^4$ CFU (HE) / ml (g). Treatment of all other infections, including candidiasis, is carried out according to the results of bacteriological studies, taking into account CFU for each pathogen.

There are publications on the results of a study of long-term complications of PID in persistent anaerobic infection with a predominant lesion of the fallopian tubes. In this regard, the optimal, especially for women with a history of infertility and miscarriage, is the inclusion in the treatment regimen of drugs with a wide spectrum of action, especially in relation to anaerobic microorganisms [4,5].

The creation of a combined antibacterial drug - amoxicillin / clavulanate - was a progressive step in the treatment of inflammatory diseases in women before and during pregnancy. The addition of clavulanic acid, while maintaining the bactericidal and safety of penicillins, significantly expanded the antibacterial activity of amoxicillin to the level of broad-spectrum antibiotics. By inhibiting the activity of bacterial beta-lactamases with clavulanic acid, amoxicillin / clavulanate is active against aerobic and anaerobic bacteria. Another important feature of amoxicillin / clavulanate is its high antianaerobic activity, similar to drugs such as metronidazole and carbapenem.

The most important aspect of the effective use of amoxicillin / clavulanate in patients with PID with infertility and miscarriage are data on the activity of the drug against aerobic and anaerobic gram-positive and gram-negative bacteria, that is, with respect to almost the entire spectrum of bacterial agents present in the vast majority of this group of women [3].

According to the instructions for use of the drug, after taking amoxicillin / clavulanate, both active substances are rapidly absorbed from the gastrointestinal tract. After taking amoxicillin / clavulanate orally at a dose of 375 mg and 625 mg C_{max} of amoxicillin in blood plasma is 3.7 and 6.5 mg / l, respectively, clavulanic acid - 2.2 and 2.8 mg / l, respectively. Plasma protein binding is 25% for clavulanic acid and 18% for amoxicillin. After a single oral administration of one tablet at a dose of 375 mg (250 mg of amoxicillin and 125 mg of clavulanic acid) or 625 mg (500 and 125 mg, respectively), approximately 60-70% of amoxicillin and 40-60% of clavulanic acid are excreted during the first 6 hours



unchanged urine. The average half-life of amoxicillin and clavulanic acid after taking the drug at a dose of 375 mg and 625 mg is, respectively, 1 hour and 1.3 hours for amoxicillin, 1.2 hours and 0.8 hours for clavulanic acid. The average half-life of amoxicillin and clavulanic acid after intravenous administration of the drug at a dose of 1.2 g and 600 mg is 0.9 hours and 1.07 hours for amoxicillin, 0.9 hours and 1.12 hours for clavulanic acid, respectively.

As a result of a comparative study of amoxicillin / clavulanate, ofloxacin, metronidazole and other antibacterial drugs by foreign and domestic authors, a high clinical (96.8%) and bacteriological (100%) efficacy of amoxicillin / clavulanate in patients with inflammatory diseases of the genitals caused by bacterial aerobic and anaerobic flora [8,9].

One of the preparations containing amoxicillin / clavulanate is Amoxiclav®. In addition to film-coated tablets for oral administration, Amoxiclav® Kviktab dispersible tablets are also produced, which have a more convenient form for resorption (do not require drinking with water), dissolve quickly, providing a high rate of drug delivery to tissues. This form and dosage with double use of the drug ensure high patient compliance.

Combined anti-inflammatory therapy regimens are actively used in preparing patients for hysterosalpingography, laparoscopy and / or hysteroscopy, that is, for all invasive procedures that are performed when examining women with infertility and miscarriage.

It is equally important to carry out active rehabilitation of patients with infertility and miscarriage after laparoscopic surgery for adhesions in the small pelvis, impaired patency of the fallopian tubes, with confirmed endometritis [2].

Antibiotic therapy is carried out in combination with estrogen-progestogen drugs, which are prescribed for 3–6 months. Against the background of these drugs during menstruation, antibacterial and antimycotic therapy is prescribed, taking into account laboratory tests that were carried out before the operation. Against the background of estrogen-progestational drugs, it is advisable to recommend also physiotherapy or balneotherapy.

The question of the possibility of pregnancy is decided after receiving negative results of examination for previously identified infections, taking into account the rules for taking material for laboratory research methods [5].

Algorithm for the treatment of women with infertility and miscarriage

Thus, after clinical and laboratory examination and accurate diagnosis, therapy in patients with miscarriage and infertility is carried out in stages, given that several causes of reproductive dysfunction can be identified in one patient simultaneously [7].

Stage I - after confirming the diagnosis of an infectious lesion of the genitals, pathogenetically justified therapy is prescribed to both spouses until the absence of laboratory signs is confirmed.

Stage II - treatment of organic pathology of the genitals (laparoscopy, hysteroscopy). These are patients with tubal peritoneal infertility, endometriosis / adenomyosis, tumors of the uterus and ovaries, intrauterine pathology in the form of intrauterine septa, synechiae and submucous myoma.

Stage III - drug therapy for the effects of adhesions, genital endometriosis, correction of endocrine disorders and disorders of menstrual reproductive function.

Stimulation of ovarian function by direct and indirect ovulation stimulants is indicated only after hormonal examination and in cases where the doctor is sure that all organic causes of infertility or miscarriage have been eliminated.

A difficult clinical situation is the development of inflammatory diseases during pregnancy. In accordance with modern data, beta-lactams can be prescribed to different categories of patients, in particular to pregnant women, in whom, due to potential toxicity, it is impossible to use antibiotics of other groups. Amoxicillin / clavulanate can be prescribed during pregnancy, in particular for the treatment of asymptomatic bacteriuria and pyelonephritis. The effectiveness and safety of this drug was confirmed by O.I. Mikhailova et al. (2013) in pregnant women with urinary tract infections.

CONCLUSION

It should be noted that women with a history of PID, as well as infertility and miscarriage are among the most difficult group of patients who have difficulties in restoring and maintaining reproductive function. Despite careful examination and treatment, problems often arise not only at the stage of preparation for pregnancy: the consequences of PID can manifest themselves both during pregnancy and in the postpartum period.



LITERATURE

1. Dunaif A., Thomas A. Current concepts in the polycystic ovary syndrome. *Annu Rev Med* 2001; 52: 401—419.
2. Sammour A., Bilijan M.M., Tan S.L., Tulandi T. Prospective randomized trial comparing the effects of letrozole and clomiphene citrate on follicular development, endometrial thickness and pregnancy rate in patients undergoing superovulation prior to intrauterine insemination (IUI) // *fertile. And Steril.* – 2001. – vol.76 – P.111.
3. Kurbaniyazova M.Z., Matrizayeva G.D., Duschanova Z.A., Saparbayeva N.R. *Central Asian Journal of Pediatrics*, 2019; 2(2): 23. <https://uzjournals.edu.uz/pediatrics/vol2/iss2/23>;
4. Доброхотова Ю. Э., Матризаева Г.Д., Курбаниязова М.З., Дусчанова З.А., Сапарбаева Н.Р., Икрамова Х.С. *Евразийский вестник педиатрии*, 2020; 2(5): 43-49 [Dobroxotova Yu. E., Matrizayeva G.D., Kurbaniyazova M.Z., Duschanova Z.A., Saparbayeva N.R., Ikramova X.S. *Evrazijskij vestnik pediatrii*, 2020; 2(5): 43-49]. <https://cutt.ly/DveOv0M>;
5. Курбаниязова М.З., Сапарбаева Н.Р. *Проблемы биологии и медицины*, 2018; 4 (104): 68-70 [Kurbaniyazova M.Z., Saparbayeva N.R. *Problemy biologii i mediciny*, 2018; 4 (104): 68-70];
6. Kurbaniyazova Madina Zafarjanovna, Bekbauliyeva Gulistan Niyetbayevna / *International Virtual Conference on Innovative Thoughts, Research ideas and inventions in sciences/ Hosted from Newyork, USA January 20th 2021 158-162 page/* <http://euroasiaconference.com>
7. Madina Kurbaniyazova , Gulistan Bekbauliyeva / *Somatic and hormonal profile of infertile women with chronic anovulation/* <https://turkijphysiotherrehabil.org/pub/pdf/322/32-2-530.pdf>
8. Orviet R., Homburg R. Chronic ultra-low dose follicle-stimulating hormone regimen for patients with polycystic ovary syndrome: one click, one follicle, one pregnancy. *Fertil Steril.* 2009; S1: 1533-1539.
9. Palomba S., Fallo A., Zullo F. Strategies for managing ovulation induction in women with PCOS and known clomiphene citrate resistance. *Curr Opin Obstet Gynecol.* 2009; 21: 465-473.
10. Amsterdam ESHRE / ASRM - Sponsored 3rd PCOS Consensus Working Group Consensus on Women's Health Aspects in Polycystic Ovary Syndrome (PCOS). *Buzz Reprod.* 2012; 27: 14-24