



Impact of pelvic inflammatory diseases on the effectiveness of assisted reproductive technologies (Literature review)

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ABSTRACT

TCDD is complicated due to the frequent absence of symptoms and diversity of clinical picture, rare occurrence of classical forms, latent course in the acute phase of the inflammatory process, predominance of chronic forms, as well as primary-chronic forms and persistent recurrent course [2, 3]. TCDD is a serious risk factor for women's reproductive health, causing the development of chronic pelvic pain syndrome, adhesions, pregnancy failure, infertility and ectopic pregnancy [4]. The frequency of tubal-peritoneal infertility increases with recurrent course of TCDD. Pelvic inflammatory diseases of the pelvic organs (PID) is a nadnozologic concept that includes all varieties of inflammatory diseases of the upper genital tract in women. UGTTs are a major part of gynecological morbidity, accounting for >65% of outpatient visits in women; the peak incidence (4-12%) is at a young age (17- 25 years), of which about 30% require hospitalization [1].

Keywords:

Purpose: The aim of this scientific review is to demonstrate the current scientific understanding of etiopathogenesis, clinic, diagnosis and treatment of pelvic inflammatory disease.

Material and methods: Russian- and English-language scientific literature sources were analyzed.

Results. All patients with TCDD of reproductive age need prescription of hormonal contraception. The conducted study shows that the use of OCs as rehabilitation after an episode of TCDD allows to ensure not only clinical recovery of the patient, but also normalization of endocrine regulation and restoration of reproductive potential. Important points are the

duration of contraceptive use and the choice of the drug. The duration of OC prescription is determined by the patient's reproductive plans, but should be at least 6 months and continue until pregnancy planning.

Diagnosis, together with its epidemiology According to a number of authors, tubal-peritoneal infertility occurs in 8% of women who have had 1 episode of TCDD, in 20% of women with 2 verified episodes of TCDD in the history and in 40% of women with 3 episodes of TCDD [5-9]. Taking into account the steady growth of TCDD, difficulties in diagnosis, "rejuvenation" of the pathology and its significant role in the development of infertility, this makes the problem relevant not only from the medical but also from the socioeconomic point of view [10]. Therefore, the aim of our

study was to search for therapeutic strategies to reduce the frequency of recurrences of TCDD.

Our data showed statistically significant improvement of the patients' condition (reduction of subjective symptoms) already on the 5th-7th day of use and normalization of laboratory data on the 10th-12th day. Probably, it is connected with the improvement of tissue permeability for local and systemic ABP. According to existing literature data, frequent relapses of both TCDD and many other chronic diseases in the absence of visible provoking factors are due to the formation of biofilms consisting of different microorganisms [13]. Russian researchers indicate that hyaluronidase, possessing enzymatic activity, is able to destroy bacterial films [13, 14]. Recent studies have shown that bovjaluronidase azoximer (750 IU/mL, 2 h incubation) provides destruction of the matrix of mature bacterial biofilms of Gram-positive (*Staphylococcus aureus* and *Enterococcus faecalis*) and Gram-negative (*E. coli*) bacteria by 40-50% [15].

One of the main problems in the treatment of TCDD is a kind of "vicious circle" - the need for frequent use of ABP and antimicrobials for elimination of 1 infectious agent leads to aggravation of dysbiosis and growth of other pathogens, which serves as a reason for aggravation of existing disorders [16, 17]. At the same time, the statistically significantly higher frequency of microbial landscape improvement and a high degree of vaginal cleanliness in the patients of the main group, noted in our study, together confirm another effect of azoximer bovjaluronidase described by the Russian authors - it is the prolongation of the action of ABP.

Another problem in the therapy of TCDD is the mixed nature of infection and high frequency of uncontrolled repeated use of ABPs with a natural increase in resistance to them. The possibility of overcoming this problem has now appeared in the form of the use of azoximer bovjaluronidase preparation - an immunomodulator, detoxicant, antioxidant with its own anti-inflammatory properties. This is confirmed by the results of our study, demonstrating a reliable decrease in the frequency of exacerbations in the patients of the

main group. According to the Russian authors, this drug weakens the course of the acute phase of inflammation, regulates the synthesis of inflammatory mediators, increases the body's resistance to infections, normalizes humoral immunity.

Statistically significantly more frequent pregnancy in the main group can be explained by antifibrotic, anti-inflammatory and antioxidant action, which can improve the state of the endometrium and ensure pregnancy. It is important to remember that bovjaluronidase azoximer does not have antigenic properties, mitogenic, polyclonal activity, does not have allergic, mutagenic, embryotoxic, teratogenic and antioxidant effects.

allergic, mutagenic, embryotoxic, teratogenic and carcinogenic effects [18]. Thus, our results indicate that the use of bovjaluronidase azoximer increases the effectiveness of complex therapy of exacerbations of chronic STD. The expediency of inclusion of bovjaluronidase azoximer in the scheme of standard ABT of TCDD is due to its high efficacy, good tolerability, optimal bioavailability, ability to create high levels of ABP concentrations in the organs of the reproductive system.

TCDD are polymicrobial infections, as they are caused by various infectious agents, the degree of virulence of which serves as one of the decisive factors influencing the prevalence of the pathological process. In modern medical science, about 2500 different infections are known. Theoretically, a woman can fall ill with any of them [5, 6]. The most frequent causative agents of genital inflammatory processes are currently *Neisseria gonorrhoeae*, *Chlamydia trachomatis*. However, a number of researchers believe that the incidence of STIs associated with gonococcal infection tends to decrease, while the incidence of non-gonococcal STIs is increasing (Tables 1, 2). In this regard, it is worth noting the importance of *Escherichia coli* in the development of TCD. Nonpathogenic *E. coli* bacteria, which normally inhabit the intestine in large numbers, can nevertheless cause the development of pathology when they enter other organs or cavities of the human body (vaginitis, cervicitis) [5, 6]. Studies performed in Finland indicate that *E. coli* and

Haemophilus influenzae were the most significant aerobic microorganisms in patients with TCDD. E. coli can rapidly acquire drug resistance. In some cases, virulent strains also cause hemolytic-uremic syndrome, peritonitis, mastitis, sepsis, and gram-negative pneumonia [11-13]. The ascending route of infection is predominant in the genesis of inflammatory diseases of the reproductive system. The penetration of infectious agents into the upper parts of the genital system occurs with the help of spermatozoa, trichomonads, passive transport of microorganisms is possible [6, 5]. Both obstetric and gynecologic inflammatory diseases are caused by the same microbial agents, affect the same organs of the female reproductive system. TCDD can be a consequence of both complications of the gestational period, and abortion, various surgical interventions on the female genital organs. Classification of TCDD, as a rule, is presented according to several parameters (etiology, clinical course, localization). According to the clinical course, the following are distinguished: acute; subacute; chronic (in remission or exacerbation) inflammatory diseases (Table 3) [1, 2, 6].

According to a number of researchers, the classification of acute salpingoophoritis, which reflects the integrity of the links of a single pathogenetic chain of the inflammatory process, is of practical use: I. Acute endometritis and salpingitis without signs of inflammation of the pelvic peritoneum.

II. Acute endometritis and salpingitis with signs of peritoneal irritation.

III. Acute salpingoophoritis with occlusion of fallopian tubes with development of tuboovarian formation. IV. Rupture of tuboovarian formation [16, 17]. Diagnosis of TCDD presents certain difficulties due to the variety of clinical forms with similar symptomatology. In recent years, there have been significant changes in the clinical course of TCDD. The frequent absence of pronounced clinical manifestations and a significant disorder of the general condition create additional difficulties in the early recognition of the acute stage of the disease. Temperature reaction, pain on palpation of the abdomen,

increased acute-phase blood parameters have become optional symptoms. At present, a sterile or progradient course of inflammatory diseases of the uterine appendages is observed in 25.7% of cases. There are certain criteria for diagnosis. A number of researchers have identified several of the most important diagnostic criteria for TCDD (Table 4) [3, 5, 15, 18].

The scope of diagnostic investigation in TCDD includes a complex of clinical, laboratory and diagnostic methods (Table 5).

Ultrasound examination (USI) of the pelvic organs is a routine method that allows a clear verification of the diagnosis and the choice of adequate tactics (Fig. 1). The presence of pelvic ultrasound evidence of hydrosalpinx is considered to be the basis for targeted search for inflammatory changes in other organs of the female reproductive system [16, 17].

The scope of treatment measures in patients with TCDD includes the use of both operative and conservative methods of treatment [1-3, 6, 18]. The algorithm of differentiated approach to the tactics of management of patients with TCDD at the stage of inpatient treatment is shown in Fig. 2 [5, 6].

Pain in chronic forms of TCDD is particularly difficult for differential diagnosis, which should be distinguished from pain due to the presence of:

- endometriosis, Allen-Masters syndrome;
- diseases of the nervous system (sciatica, osteochondrosis) and urinary system;
- pathology of the gastrointestinal tract (colitis, diverticulitis, tumors);
- traumatic injury to the spine;
- abdominal prolapse;
- "chronic fatigue syndrome", etc. [1, 2, 4, 6].

Currently, pelvic inflammatory diseases (PID) are leading in the structure of gynecologic pathology, which are most often diagnosed in women of active reproductive age.

PIDD unites a group of pathological conditions with close localization of the pathological process and similar basic clinical and laboratory signs. Modern features of the course of TCDD consist in the absence of a bright manifestation of the disease and runs as a primary chronic

process with a long recurrent course, as well as low effectiveness of drug therapy [8, 9]. In this regard, timely diagnosis and assessment of the severity of the inflammatory process is difficult for clinicians. The outcomes of an episode of TCDD are often chronic course of the inflammatory process, chronic pelvic pain syndrome, ectopic pregnancy, and infertility [2, 10, 11].

Currently, the methods of diagnostics and treatment of TCDD are well developed [8, 12, 13]. According to modern studies, therapy of TCDD should be prescribed empirically with antibacterial drugs with a wide coverage of the spectrum of probable pathogens [14].

According to V.E. Radzinsky (2017), a common mistake in the management of patients with TCDD is the neglect of rehabilitation, due to which even after rational antibacterial therapy there is a high probability of chronicization of the inflammatory process, recurrences and reproductive failures [10]. Structural and functional disorders play an important role in the pathogenesis of TCDD not only at the local but also at the systemic level [10, 15]. There are only some studies in the literature devoted to methods of rehabilitation of patients with this pathology [16].

Conclusion . It is necessary to give preference to drugs with high contraceptive efficacy, minimal side effects (no effect on weight) and the presence of additional positive effects (antiandrogenic, antimineralocorticoid). The drug of choice may be a low-dose monophasic preparation containing 30 mcg of ethinylestradiol and 3 mg of drospirenone (Midiana®).

The treatment of inflammatory diseases of the genitalia includes a different range of therapeutic procedures. For this purpose, many methods of drug and non-drug therapy are used, taking into account clinical manifestations, laboratory diagnostic data [1, 2, 11]. Therapeutic tactics should be aimed primarily at controlling clinical symptoms, eradication of the causative agent and minimizing the risks of distant consequences, which develop in almost 1/4 of patients. In recent years, the CDC (Center for Disease Control, USA) recommends adhering to a "low threshold" for the initiation of

aggressive therapy of acute pelvic inflammatory processes, it is also suggested to treat all sexual partners with whom women have had sexual contact 60 days before the onset of symptoms of TCDD. Since 2010, it is recommended that all patients with TCDD be offered HIV screening. If sexually transmitted infections (STIs) are present sexually transmitted infections (STIs) as a cause of TCDD, re-testing for infection is performed 3-6 months after treatment completion, taking into account the high risk of reinfection, including from an untreated sexual partner [15, 16].

When prescribing antibiotics, it is important to remember the mixed nature of pelvic infection. It is usually not possible to accurately determine the etiologic composition of the infection for the following reasons:

- material from the fallopian tubes can only be obtained surgically;
- vaginal flora examination does not accurately convey the composition of pathogens in the upper genital tract;
- microbiologic (culture) examination is time-consuming and is not suitable for the detection of anaerobes and chlamydia.

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