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## TUBAL FACTOR AS ONE OF THE LEADING FACTORS OF FEMALE INFERTILITY

Infertility is one of the most urgent problems of today, as this condition makes it impossible for a mature organism to produce offspring. The issue of restoring and maintaining reproductive health is one of the priority issues of modern gynecology and reproductive medicine. The article adduces the main etiological and pathogenetic links of tubal-peritoneal infertility, as well as briefly presents modern views on the diagnosis and treatment of women in this group.

**Conclusion.** The analysis of current data on the treatment of tubal obstruction will provide an opportunity to more rationally address the issue of choosing to restore their patency.

**Key words:** tubal factor; infertility; assisted reproductive technologies.

### ТРУБНЫЙ ФАКТОР КАК ОДИН ИЗ ВЕДУЩИХ ФАКТОРОВ ЖЕНСКОГО БЕСПЛОДИЯ

Бесплодие является одной из наиболее актуальных проблем, поскольку данное состояние делает невозможным способность зрелого организма давать потомков. Вопрос восстановления и сохранения репродуктивного здоровья является одной из приоритетных проблем современной гинекологии и репродуктологии. В статье освещены основные этиологические и патогенетические звенья трубно-перитонеального бесплодия, а также кратко представлены современные взгляды на диагностику и лечение женщин данной группы.

**Вывод.** Представленный в статье анализ современных данных по лечению трубной непроходимости даст возможность более рационально решать вопросы выбора восстановления их проходимости.

**Ключевые слова:** трубный фактор; бесплодие; вспомогательные репродуктивные технологии.

### ТРУБНИЙ ФАКТОР ЯК ОДИН ІЗ ПРОВІДНИХ ЧИННИКІВ ЖІНОЧОГО БЕЗПЛІДДЯ

Безпліддя є однією з найбільш актуальних проблем сьогодення, оскільки даний стан унеможлиблює здатність зрілого організму давати нащадків. Питання відновлення та збереження репродуктивного здоров'я є однією із пріоритетних проблем сучасної гінекології та репродуктології. У статті висвітлено основні етіологічні й патогенетичні ланки трубно-перитонеального безпліддя, а також коротко представлено сучасні погляди на діагностику та лікування жінок даної групи.

**Висновок.** Проведений аналіз сучасних даних щодо лікування трубної непрохідності дасть можливість раціональніше вирішувати питання вибору відновлення їх прохідності.

**Ключові слова:** трубний фактор; безпліддя; допоміжні репродуктивні технології.

Infertility is a complex medical and social problem that has been one of the most urgent in modern obstetrics, gynecology and reproductive medicine for many years [1]. According to the WHO, the frequency of infertile marriages ranges from 8 to 30 % and does not tend to decrease in all countries. In Ukraine, the frequency of infertile marriage among married couples of reproductive age is more than 15 %, in some regions this figure is close to 20 % – a level that is defined as critical and has a negative impact on demographics [2]. The cause of infertile marriage in 40–50 % of cases is the pathology of the reproductive system in one of the partners, less often – in 25–30 % – in both [3, 4]

According to WHO recommendations, infertility should be predicted and examination and treatment of patients should be started immediately if there is no pregnancy within 12 months of active sexual life in patients under 35 years, within 6 months in patients after 35 years, in men over 40 years [5]. Diseases of the fallopian tubes in the structure of female infertility are 29.5–83 % [3, 6].

In primary infertility, the incidence of fallopian tubes is 28.5–71 %, in secondary infertility – 43–83.1 % [7]. Factors of secondary infertility include gynecological surgery history; complications after abortion; inflammatory diseases of the pelvic organs, age and improper lifestyle.

The main cause of tubal infertility is considered to be inflammatory diseases history of the female genital organs

and sexually transmitted infections, which lead to complete or partial obstruction of the tubes due to irreversible damage to the cylindrical epithelium of the fallopian tubes, wall obliteration, infiltration, flexure due to peritubular and ovarian adhesions [8]. The reasons for the formation of partial or complete violation of the patency of the fallopian tubes also includes the adhesion process. [9]

Surgical interventions on the pelvic organs and abdominal cavity, by laparotomy, are a high risk group for the formation of tubal infertility [3]. According to the WHO, unilateral or bilateral occlusion of the fallopian tubes can occur in 15 % of patients after appendectomy, in 60–80 % of patients after ovarian surgery, conservative myomectomy, due to tubal pregnancy [9].

In the structure of tubal-peritoneal infertility, the tubular factor is 29.5–83 %, and the peritoneal form of infertility is observed in 9.2–34 % [10]. In patients with tubal-peritoneal infertility for more than 4 years in the presence of tubal patency, only peritoneal infertility was found in 58–70.5 % of cases. Tubal-peritoneal infertility occurs in 30–32.7 % of patients with PCOS [10].

After a single episode of salpingitis, fallopian tube obstruction occurs in 11–13 %, after a double – in 23–36 %, when three or more exacerbations – in 54–75 % of cases [10]. In 43 % of women who have suffered from inflammatory diseases of the uterine appendages, there is complete

obstruction of the fallopian tubes, and in 49 % of cases – partial. [12]

Adhesions that occur after the primary inflammatory lesion of the fallopian tubes disrupt the mechanisms of capture and transport of the egg [7].

Tubal factor infertility occurs when a sperm cannot enter the fallopian tube and then the ovary to fertilize an egg, or it is impossible for a fertilized embryo to enter the uterus. The fallopian tubes connect the ovaries to the uterus on two sides.

Tubal infertility is divided into two types: voluntary – as a consequence of sterilization of tubes, and forced – as a consequence of tube disease and their partial or complete obstruction. In turn, the forced is divided into proximal – the obstruction of the tube closer to the uterus. According to the ASRM, proximal tubal occlusion is from 10 % to 25 % of tube diseases and is usually a relatively mild condition for treatment. Distal – obstruction closer to the ovary, as well as complete obstruction of the fallopian tubes [13].

Fimbria is a finger-shaped edging of tissue that helps an unfertilized egg enter the fallopian tube. Damage to the fimbriae can prevent the egg from passing from the ovary into the fallopian tubes.

Damage to the fallopian tube and tubal factor infertility are common consequences of the upper genital tract infection – Chlamydia trachomatis. This pathogen has a direct cytotoxic effect on the mucous membrane of the human fallopian tube, which leads to loss of microvilli and disruption of cellular connections associated with the rupture of epithelial cells [14].

Histological examination of the fallopian tubes and endometrium in patients with tubal-peritoneal infertility of inflammatory origin reveals the accumulation of acidic and neutral mucopolysaccharides, small-point infiltrates along the vessels, "lymphoid aggregates" in the endometrium. Restructuring of microcirculation in the fallopian tubes in patients with tubal-peritoneal infertility of inflammatory origin in the first 2 years is characterized by the development of arteriole sclerosis, blood bypass, venules hypertrophy. The result is atrophy of the smooth muscle cells of the fallopian tubes, sclerosis of the venule wall, leading to decompensation of venous blood flow and varicose veins in the isthmus part of the fallopian tubes. Sometimes in tubal-peritoneal infertility of inflammatory genesis, immunological homeostasis is violated, and antibodies to uterine, fallopian tube, and ovarian tissues appear [10].

Recommendations for selecting a method for diagnosing fallopian tubes in patients with tubal infertility initially include a baseline assessment with chlamydial antibody testing and tuberculin polymerase chain reaction (TBPCR) in endemic areas with a high prevalence of the disease [10].

Briceag I. and Costache A. et al (2015) suggest that if tubal infertility is suspected, women who do not know if they have comorbidities should be offered hysterosalpingography as an initial screening test; alternatively, hysterosalpingography should be replaced by hysterosalpingo-contrast-ultrasonography – it is a fluoroscopic visualization of the uterine cavity and fallopian tubes by injection of radiopaque contrast agents. Tubal spasm is to blame for the lower accuracy of this diagnostic technique, but with the use of intravenous scopolamine and patient rotation, it was minimized [15]. This method allows detecting malformations and hypoplasia of the uterus, hyperplastic processes of the endometrium, adhesions in the pelvis.

However, Ngowa J. D, Kasia J. M. et al (2015) after a number of studies state that hysterosalpingography has limited diagnostic value in tubal factor infertility and has low diagnostic value for pelvic adhesions. It is believed that laparoscopy should be performed in cases of abnormal hysterosalpingograms and even in cases of normal hysterosalpingograms in the context of unexplained infertility [16].

Laparoscopic chromopertubation remains the gold standard in assessing tube patency. By injection of diluted indigo carmine is injected into the uterine cavity with simultaneous laparoscopy to visualize the filling of the tubes and effusion into the abdomen. The disadvantages of this procedure are: cost, invasiveness and analgesia [15]. During laparoscopic intervention, it should be taken into account that under the influence of bipolar coagulation there is a premature attenuation of ovarian function due to protein denaturation (the initial stage of denaturation begins with heating the ovarian tissues to a temperature of 45 ° C). This situation leads to a decrease in ovarian reserve at a young age of patients [17].

Today, the method of mechanical clipping of the proximal part of the fallopian tubes is used, but the disadvantage is that the volume of inflammatory exudate can increase due to the lack of drainage [17].

The problem of treatment of patients suffering from tubal infertility does not lose its relevance, despite the wide arsenal of drugs and significant progress in the use of endoscopic techniques of adhesiolysis and restoration of fallopian tubes. [7]

There are two main methods of treating tubal factor infertility – surgical and conservative therapy to repair a damaged tube. If these methods are not effective, IVF is usually performed to achieve pregnancy.

The most effective drugs for conservative treatment are the etiological therapy of chlamydia – tetracycline antibiotics, erythromycin and amoxicillin. In case of torpid and chronic processes, nonspecific immunotherapy is prescribed. According to the indications, local therapy with antiseptic solutions is prescribed. Patients are monitored for healing 2 weeks after the end of antibiotic therapy, then the patient is monitored for 3 months with clinical and laboratory tests once a month. Parallel examination and treatment of the sexual partner is necessary. It is recommended to treat uncomplicated anogenital infections with the following drugs – Doxycycline 100 mg orally twice a day for 7 days, or Azithromycin 1 g orally in one dose. Alternatively, Amoxicillin 500 mg orally three times daily for 7 days; Erythromycin 500 mg orally four times a day for 7 days; Ofloxacin 300 mg orally twice daily for 7 days or Tetracycline 500 mg orally four times daily for 7 days [18].

According to the Special Committee of the World Congress on Fertility and Infertility, in infertility due to obstruction of the fallopian tubes, the following types of surgery are performed: salpingolysis, fimbrioplasty, salpingostomy (salpingoneostomy), anastomosis, anastomosis, implantation, and combination surgery [19].

Surgical correction is performed in the first phase of the menstrual cycle in order to provide optimal conditions for tissue regeneration and the possibility of rehabilitation measures.

Types of laparoscopic reconstructive plastic surgery:

– salpingoneostomy – restoration of patency of the fimbrial uterine tube with its complete occlusion. Birth rates after

salpingoneostomy were 20–30 % with an increase to 40 % after 50 months of supervision. Retrospective data suggest that most pregnancies occur 12–24 months after surgery [20].

- fimbrioplasty is used in the narrowing of the fimbrial uterine tube or its partial obstruction by a fibrous ring;

- ovariolysis – dissection of adhesions that create obstruction of the ovary.

- salpingolysis – dissection of adhesions surrounding the fallopian tube. This intervention was first performed in 1884. Now this operation is the most common. Surgical correction of peritubal adhesions, with minimal access, is recommended during the adhesion process of stage I-II and in the absence of distal occlusion of the fallopian tubes. Randomized surveys show that the probability of successful outcomes of tubal surgery, including the separation of adhesions, is reduced by the severity of the pathological process, being more effective than without surgery, 67 % compared with 24 % when stage I, 41 % compared with 10 % when stage II and 12 % compared to 3 % (unreliable) when stage III disease under observation for three years after surgery [20].

- uterine tube plastic surgery (English - reconstruction of uterine tube) – reconstruction and restoration of the integrity of the fallopian tube;

- salpingectomy – surgical removal of one or both fallopian tubes [13]. It is important during the preparation of a woman for ART, if there is a need for surgical removal of the fallopian tubes during laparotomy, it is necessary to perform a tubectomy proximal to the body of the uterus to avoid ectopic pregnancy in the cult of the fallopian tube during embryo transfer.

Salpingoanastomosis is a resection of a tube in which a narrowed or obliterated tube is excised, this manipulation is performed in cases where obstruction has formed in the isthmus part of the tube in the presence of patency in the ampullary and interstitial region. The tube on the polyethylene pipe is sewn “end to end”.

According to Gary S. Berger, John M. et al. (2016), the overall rate of total pregnancy after salpingo-anastomosis was 69 %. The overall birth rate was 35 % [21].

The percentage of pregnancy in women after surgery depends on many factors and is 18–57 %. Pregnancy occurred after salpingostomy and fimbrioplasty in 72 % of patients who had only periovarial fusion, in 67 % – only peritubular adhesions, in 35–50 % – peritubular and periovarial adhesions and 10–26 % of patients had hydrosalpinx [19].

At the present stage in the fight against tubal infertility, increasing preference is given to assisted reproductive technologies. The method of infertility treatment, based on in vitro fertilization of eggs and transfer of embryos to the uterus, made a revolutionary overthrow in the field of reproduction [19].

More than 99 % of ART procedures are IVF. Because the ART procedure consists of several stages over an interval of about 2 weeks, the procedure is often referred to as the treatment cycle [22].

To date, there are three main methods of assisted reproductive technologies: 1) intrauterine insemination (IUI); 2) in vitro fertilization (IVF); 3) intracytoplasmic sperm injection (ICSI).

IUI – specially prepared sperm are injected into the uterus when ovulation is expected. IVF – after mixing sperm and

oocytes, fertilization and initial fragmentation take place in a laboratory in special media. ICSI is the injection of a single sperm directly into the cytoplasm of an oocyte for fertilization [23].

The main indications for in vitro fertilization include severe fallopian tube disorders, bilateral salpingectomy.

In the IVF program, oocytes obtained under ultrasound control from ovarian follicles in cycles of controlled ovulation stimulation and specially prepared sperm are combined in the laboratory. Fertilization occurs outside the body. At different stages of fragmentation of fertilized oocytes they are transferred to the uterus (ET – embryo transfer) to wait for pregnancy [23].

The frequency of pregnancy after IVF – embryo transfer is within 30 %. According to the literature data, among pregnancies resulting from IVF, 35 % are multiple. At the same time, in 24–28 % of cases, twins were noted, in 4–6 % – triplets, and in 0.6 % – more fetuses [24].

The results of IVF and fallopian tube surgery are difficult to compare because the results vary depending on the qualifications of the surgeon and the human reproduction clinic. One randomized study showed that the surgeon as a first line of treatment is associated with lower costs and a higher overall incidence of pregnancy. Surgical preparation for IVF has several purposes. First, the elimination of the negative impact of hydrosalpinx on the processes of embryogenesis. Second, reducing the risk of ectopic pregnancy during IVF. Third, the elimination of pathology of the pelvic organs, which can adversely affect the results of IVF. However, the analysis shows that the onset of pregnancy after tubal surgery compared to IVF remains unknown – there are no randomized controlled trials comparing IVF with tubal surgery [25].

Other current data show that the active implementation of large-scale tubal operations before any IVF cycle will reduce up to 30 % of the costs associated with gaining viability in cases of tube factor sterility [15].

Prevention of tubal factor infertility is the timely detection of patients with chlamydia, gonorrhea, trichomoniasis and other sexually transmitted diseases, adequate treatment of carriers and their sexual partners, implementation of extensive health education among the population, especially among young people. Personal prevention comes down to avoiding casual sex, using condoms, female condoms, gel-based microbicides, vaginal rings, films and nanofibers, and if an infection is suspected, one must see a doctor immediately [26].

Sexually transmitted infections are still part of the global health crisis. Fighting it cannot succeed only with treatment, timely prevention is needed [26].

**CONCLUSIONS.** Today, the tubal factor is one of the main factors of infertility. In obstetrics and gynecology, there are many modern methods of diagnosis and treatment of this pathology, both conservative and surgical, but the main direction to prevent tubal-peritoneal infertility is personal prevention, which avoids accidental sexual contact, use of contraception, early detection and adequate treatment of inflammatory diseases of the female genital organs and sexually transmitted infections. If possible, avoid surgical interventions due to further formation of the adhesion process. The analysis of current data on the treatment of tubal obstruction will make **it possible to more rationally solve the issue of choosing to restore their patency.**

**PROSPECTS FOR FURTHER RESEARCH.** In order to improve the results of tubal infertility treatment, the priority ways are: development of new modern diagnostic methods, improving the effectiveness of treatment of women, improv-

ing various types of surgical treatment, diseases of this group of patients, use of assisted reproductive technologies and their widespread implementation after unsuccessful surgical treatment.

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