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DIAGNOSIS AND TREATMENT OF PATIENTS WITH INFERTILITY DEVELOPED AGAINST THE BACKGROUND OF CHRONIC PROSTATITIS

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Introduction

According to the WHO definition, male infertility is a disorder of male reproductive function, which is expressed in quantitative or qualitative changes in spermatozoa. Male infertility can be a clinical manifestation of many different pathological conditions affecting both the reproductive and other body systems. A significant share of the diversity of forms of male infertility is made up of violations of the qualitative characteristics of the ejaculate. In particular, it is known that physicochemical changes in the tissue of the prostate gland that occur during its inflammation lead to a change in the quality of sperm [1–3]. The issues of the etiology and pathogenesis of fertile dysfunction in chronic prostatitis remain the subject of serious discussions and disagreements. Despite many published works, this condition remains insufficiently studied and difficult to treat [4, 5]. Although abacterial prostatitis is recognized as an independent disease, it remains unclear whether it is a stage in the development of bacterial prostatitis. It has been suggested that primary infectious prostatitis does not exist, but only secondary infectious prostatitis, which occurs as a result of morphological changes or dysfunction of the prostate gland [6, 7]. Oxidative stress, which occurs under conditions of the inflammatory process, negatively affects the testicular microenvironment and disrupts spermatogenesis, damages DNA, reduces motility and changes the morphology of spermatozoa. Many aspects of oxidative stress are caused by damage to mitochondria, the energy potential of which is regulated, in particular, by inositols [8–10]. One of the reasons for the deterioration of fertility in patients with chronic prostatitis is a decrease in the concentration of testosterone in the blood serum. Thus, a direct correlation was established between the level of sex hormones and the severity of sexual dysfunction in men. These data indicate the important role of non-testicular androgens in regulating male sexual function [11–13]. The prostate gland and testicle are in a positive correlative relationship, and if one organ is dysfunctional, the other suffers. At the same time, the prostate gland is an organ responsible for the metabolism of sex hormones, and its disease leads to a disruption of this metabolism [14, 15]. Unfortunately, the etiology and pathogenesis, timely diagnosis of chronic prostatitis, its characteristic infertility, and therapeutic approaches to its treatment are all issues that are far from being resolved today. Despite the widespread prevalence of male infertility in patients with chronic prostatitis, the role of this disease in the genesis of

infertility remains controversial.

Purpose of the study:to evaluate the impairment of sperm quality and prostate secretion in patients with infertility and chronic prostatitis, and to compare the effectiveness of various treatment regimens for this pathology.

Material and methods

A retrospective analysis of the treatment results of patients with infertility and chronic prostatitis was performed. The reason for seeking medical help from a urologist was an infertile marriage. As a result of a comprehensive examination of patients, chronic prostatitis was verified in some patients, which had not previously manifested clinically, in some patients the presence of chronic prostatitis was confirmed anamnestically. The study included only patients who first sought medical help with problems of conception and had not previously received specific treatment. The data of laboratory examination and treatment of patients were obtained from the medical records of outpatients (form No. 025 / U-87) by the copying method.
Our analysis included 50 men of reproductive age from 18 to 36 years (mean age was 26.6±2.2 years) with chronic prostatitis, having various manifestations of pathospermia. In the 1st group (n=25), patients along with standard therapy for chronic prostatitis received a complex biologically active supplement (BAS) Aktifert-Andro according to the standard scheme (1 tablet 1 time per day for 3 months in a continuous course), in the 2nd group (n=25) - only standard drug therapy for chronic prostatitis: anti-inflammatory, antibacterial, prostatotropic, anti-edematous, improving microcirculation.
General clinical, laboratory and ultrasound examination methods were used according to generally accepted standards. All patients underwent physical examination of the prostate gland per rectum. Laboratory methods included spermogram, bacteriological examination of ejaculate samples, microscopy of prostate secretion. When conducting bacteriological analysis, a bacterial titer of at least 10 was considered diagnostically significant.^{4}CFU/ml.
The prostate gland secretion was obtained after digital massage of the prostate through the rectum. The norm was taken to be no more than 10 leukocytes per field of vision in the prostate secretion, a large number of lecithin grains and the absence of erythrocytes. The ejaculate was analyzed according to the 2010 WHO recommendations. The MarScreen method was used to detect antisperm antibodies (IgA, IgG) on the surface of spermatozoa (MAR test). Laboratory studies were performed before the start of treatment and 3 months after the start of treatment. Chronic prostatitis was diagnosed according to generally accepted criteria and standards, using the Index of the Chronic Prostatitis and Pelvic Pain Syndrome Symptom Scale in Men according to the US National Institutes of Health (NIH-CPSI).
Transrectal ultrasound of the prostate gland determined the size and volume of the prostate, its structure, symmetry, presence of additional formations, foci of increased and decreased echogenicity, calcifications and fibrosis. Statistical processing of the obtained results was carried out using the Microsoft Excel, Statistica, v. 12.6 for Windows (2015) software package with an assessment of the nature of the distribution. The reliability of differences was assessed using the Student criterion.

Results and discussion

The age structure of the patients we examined was as follows: 8 (16%) patients were under 20 years old, 15 (30%) were between 20 and 30 years old, and 27 (54%) were over 30 years old. That is, the incidence of chronic bacterial prostatitis increases with age.

Normal prostate size (less than 20 cm^3) were determined in 26% of patients, moderately enlarged (20–30 cm^3) - in 56%, significantly enlarged (more than 30 cm^3) — in 18%. Initially, the groups were comparable in terms of the laboratory parameters studied.
According to the results of bacteriological analysis of ejaculate, in 39 patients the titer of bacteria in the culture exceeded 10^4CFU/ml, in 11 patients the growth of microflora was not detected or was detected in a clinically insignificant titer (less than 10^4CFU/ml).
When comparing laboratory parameters of prostate secretion and ejaculate in different age groups of patients, the following trend was noted: the most pronounced inflammatory changes in the ejaculate were detected in patients aged 20–30 years; in patients younger than 20 years, inflammatory changes were slightly less pronounced and occurred less frequently; and in the group older than 30 years, inflammatory disorders were most common, but their severity corresponded to the average level (Table 1).

Таблица 1. Характеристика отклонений лабораторных показателей у пациентов с хроническим простатитом в различных возрастных группах

Лабораторный показатель	Моложе 20 лет (n=8)	20-30 лет (n=15)	Старше 30 лет (n=27)
Среднее содержание лейкоцитов в сперме, млн/мл	2,4	4,7	1,1
Среднее содержание лейкоцитов в секрете простаты, клеток в поле зрения	96,4	88,2	34,5
MAR-тест, %	74,6	58,9	42,1

Changes of an inflammatory nature in the prostate secretion were most pronounced in young patients (under 20 years old); at an older age (20–30 years old), the activity of inflammatory changes somewhat decreased, reaching its minimum in patients over 30 years old. A similar trend was maintained when evaluating the MAR test: its indicator decreased from 74.6% (in the group under 20 years old) to 42.1% (in the group over 30 years old).
With increasing age, the frequency and prevalence of detected deviations in laboratory parameters increased, but their activity and severity tended to decrease. The detected changes allow us to conclude that the number of leukocytes in the prostate secretion and ejaculate does not fully reflect the state of the prostate gland and does not provide complete information for understanding the nature of the current inflammatory process. The fact is that when collecting biological material for these tests, only part of the prostate acini is emptied, which cannot give a complete picture of the inflammatory process in the gland, but characterizes the state of a limited area of the organ.
Despite the lack of clear patterns in the combination of microbiological, immunological and spermatological changes in prostate secretion and ejaculate, these methods are the “gold standard” for diagnosing pathological conditions of the reproductive system due to their low cost, availability and speed of execution.
An assessment of the relationship between inflammatory disorders (according to laboratory tests) and structural changes in the prostate gland revealed the following patterns. With an increase in the size of the prostate in patients with chronic prostatitis, a decrease in the severity of inflammatory changes in the prostate secretion and ejaculate is noted, which may be due to the replacement of gland tissue with connective tissue during a chronic inflammatory process in the tissue of the organ itself. It is known that a moderate increase in the prostate indicates its edema, which is a sign of an inflammatory process and the activity of which is characterized by inflammatory abnormalities in laboratory tests. A significant increase in the size of the prostate gland is caused not by edema of the organ, but by cicatricial structural changes in the tissue of

the gland itself, which is a sign of a chronic sluggish process without exacerbations. This is reflected in a decrease in the severity of inflammatory changes in the prostate secretion and ejaculate with an increase in the size of the gland.
Initially, oligoasthenozoospermia was detected in 18 patients (72%) in the 1st group, and in 20 patients (80%) in the 2nd group. The patient groups were compared mainly by the severity of inflammatory changes in the prostatic secretion and ejaculate. After a three-month course of treatment, leukospermia and erythrocytes were absent in the ejaculate of 52% of patients in both groups. The level of inflammatory abnormalities was minimal in the remaining men (weak leuko- and erythrospermia were detected). In the 1st group, the general parameters (viscosity, liquefaction time, color, impurities) were normal in almost all patients, as well as the morphology and viability of spermatozoa (Table 2). Mild agglutination of spermatozoa was detected in 6 cases, mild asthenozoospermia was present, aggregation was absent, and the MAR test was negative. The severity of inflammatory changes in the prostate secretion was minimal. Only isolated cases of severe (more than 50 leukocytes in the field of vision) — in 1 (4%) person and moderate (10–50 leukocytes in the field of vision) — in 3 (12%) people of inflammatory changes in the prostate secretion were revealed. In other cases, the indicator corresponded to the norm. Among the patients of the 2nd group, the presence of mucus in the ejaculate and a shift in the pH of the ejaculate, an increase in the viscosity of the sperm and an increase in the time of its liquefaction were more often noted (see Table 2).

Таблица 2. Выявляемость сперматологических отклонений в группах

Показатель	1-я группа, %		2-я группа, %	
	До лечения	*После лечения*	*До лечения*	*После лечения*
Изменения общих показателей (вязкость, pH, время разжижения, цвет, примеси)	21	4	23	8
Олигоастенозооспермия	18	6	20	12
Лейко(эритро)спермия	12	2	14	7
Патоспермия	11	5	15	8
Агрегация, агглютинация	16	4	14	7
Положительный MAR-тест	8	-	7	5

Asthenozoospermia was also more pronounced, in some cases oligoastheno- and teratozoospermia were detected, agglutination and aggregation of spermatozoa, weakly positive (50-60%) MAR-test were recorded more often. The differences were statistically significant ($p<0.05$). Inflammatory phenomena (0.5-6 million leukocytes in 1 ml of ejaculate) were detected in the spermogram of 7 patients, accompanied by pathospermia and asthenozoospermia, mucus admixture and shift in pH of the ejaculate, the MAR-test was at the level of 50%. Inflammatory changes and microbiological abnormalities in laboratory tests of prostate secretion in the 2nd group were significantly more common than in the 1st group ($p<0.05$). Pronounced inflammatory changes in the prostate secretion were detected in 5 (20%) patients, moderate ones - in 7 (28%). In other cases, no deviations of this indicator were detected.
As can be seen from the presented data, the complex dietary supplement Aktifert-Andro contributed to the improvement of the qualitative and quantitative parameters of the ejaculate, as well as to the improvement of the sperm quality. The components included in Aktifert-Andro (myo-inositol, carnitine, arginine, cysteine, selenium, zinc, vitamin E and folic acid) help to

reduce the viscosity of the ejaculate, increase the activity and motility of sperm. Myo-inositol is involved in the synthesis of proteins necessary for the maturation of sperm. In addition, it regulates the osmolarity and volume of seminal fluid, increasing the motility of sperm. The complex effect on the reproductive function of men, the ability to eliminate existing fertile disorders provide grounds for the use of this drug on a planned basis for the purpose of pre-gravid preparation, including in men with chronic prostatitis. Inositols are traditionally used as a means of treating female infertility associated with insulin resistance. However, recently there is evidence of their use in the treatment of male infertility. In particular, clinical algorithms are proposed for patients with asthenozoospermia [16]. In European studies, an improvement in sperm motility was noted in 85.3% of patients after a three-month course of treatment with myo-inositol-based drugs with minerals and vitamins [17]. This component is a sugar-like molecule and is one of the precursors for the synthesis of phosphatidylinositol polyphosphates, key biomolecules belonging to the signaling system of several cellular functions. Myo-inositol normalizes the metabolic profile of patients, increasing insulin sensitivity, improves sperm characteristics such as sperm concentration, motility and morphology, i.e. it can be used in the treatment of spermatological and metabolic disorders responsible for male infertility [18].

Conclusion

Chronic prostatitis complicated by infertility is most common in the age group over 30 years, while the activity of the inflammatory process is more pronounced at a young age of up to 20 years. The study revealed that with an increase in the size of the prostate gland, the severity of inflammatory changes in the prostate secretion and spermogram decreases, which may be due to a change in the structure of the organ and the replacement of glandular tissue with connective tissue. The detected microbiological and spermatological changes in the prostate secretion and ejaculate in different age groups in patients with chronic prostatitis and infertility are of the same type. Inclusion of the Aktifert-Andro complex in the complex therapy of male infertility developed against the background of chronic prostatitis allows affecting various links in spermatogenesis disorders, which is especially important given the polyetiology of this pathology.

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