

OXIDATIVE STRESS AND MALE INFERTILITY

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ABSTRACT: Male infertility is a polyetiological disease. In modern urology, the issue of effective correction of pathospermia remains relevant. So, if a patient has varicocele, hypogonadism, or infection of the accessory gonads, the tactics of a urologist are determined and beyond doubt. At the same time, the issue of treatment of idiopathic male infertility remains open. Modern publications in most cases point to the use of supplements containing antioxidants, however, the effectiveness of this technique is not defined as high, nor are the types and dosages of antioxidants defined.

KEYWORDS: Infertility, men, patients, stress, infection, treatment, drugs.

INTRODUCTION

In the modern world, the problem of solving the issue of infertile marriage has gone far beyond the scope of only medical activity. Currently, infertility in marriage is an important aspect of the socio-demographic policy of any state, including our country. According to the World Health Organization, infertility in marriage is the absence of a desired pregnancy after 12 months (or six months in the case of a spouse over 35 years of age) of regular intercourse without contraception. A group of WHO experts set a threshold of 15%, at which the government should consider infertility in marriage as the most important medical and social problem, which will further determine demographic policy.

For a long time, infertile marriage was mostly considered in the context of female infertility [1]. But at present, the proportion of male infertility has increased significantly. In the structure of infertile marriage, the male factor occurs in almost half of the cases, and it is expected that its share will increase. This is especially evident against the background of a progressive decrease in the concentration and total number of spermatozoa over the past decades, an analysis of publications from 1973 to 2011 indicates a decrease in the average concentration of spermatozoa by 52.4% [2]. The study of the problem of male infertility is connected not only with the solution of the reproductive issue. Patients with an established diagnosis of male infertility have a higher predisposition to diabetes mellitus, coronary heart disease, depression, alcohol abuse and drug addiction compared to fertile men. In addition, data from published studies show a higher risk of

developing testicular cancer, prostate cancer, lymphoma, and breast cancer in infertile men compared to healthy individuals [3].

In urology, methods of treating conditions such as: infections of the accessory glands of the reproductive system (inflammatory nonspecific diseases of the prostate gland – prostatitis, seminal vesicles – vesiculitis, appendages of the testicles – epididymitis), varicocele, hypogonadotropic hypogonadism have been developed and proven effective. Despite a large number of studies and achievements of modern urology, a high incidence of idiopathic infertility remains, the proportion of which is 30-40% . Unlike unexplained male infertility with its normal sperm parameters, idiopathic male infertility is diagnosed in the presence of altered sperm characteristics without an identifiable cause and the absence of a female infertility factor [4]. Among the drugs used to treat idiopathic male infertility, the most common are: hormonal drugs, antioxidants and combination therapy. At the same time, currently none of the modern methods of treatment has shown sufficient effectiveness in the empirical therapy of the idiopathic form of male infertility. Therefore, the search for possible causes leading to pathospermia and ways to correct them is one of the most relevant in urology. The connection of idiopathic infertility with such factors as an unhealthy lifestyle, unfavorable environmental conditions and factors of industrial production is actively discussed in the literature. With biological enhancement, i.e. simultaneous exposure to these factors, the probability of sperm damage increases [5].

Oxidative stress damages the plasma membrane of spermatozoa, impairing its fluidity, and also violates the integrity of the nuclear and mitochondrial genome of spermatozoa. In this connection, the most common cause of a decrease in the fertilizing ability of spermatozoa against the background of oxidative stress is the rupture of DNA molecules, more commonly known as fragmentation of sperm DNA, which can be single-stranded or double-stranded. With a high level of fragmentation of sperm DNA, the probability of pregnancy in the natural cycle decreases by 6.5-10.0 times. At the same time, it is worth noting that studies have shown the absence of a significant correlation between the level of pathospermia and fragmentation of sperm DNA, so in at least 15% of cases, patients with normozoospermia are infertile due to an increase in the level of fragmentation of sperm DNA. In the human body, there are internal and external antioxidant mechanisms necessary to counteract the high level of reactive oxygen species. Endogenous antioxidants consist of enzyme antioxidants such as superoxide dismutase, catalase, thiol peroxidase, and non-enzymatic antioxidants such as glutathione. The exogenous antioxidant system includes vitamin A, vitamin C, vitamin E, L-carnitine, N-acetylcysteine, selenium and zinc, which must enter the body from the external environment in order to maintain a delicate balance between oxidation and reduction in any living cell [6].

A modern man is often subject to an unhealthy lifestyle: eating disorders, physical inactivity, leading to obesity, which causes a systemic inflammatory reaction, increased production of adipokines, cytokines and high levels of reactive oxygen species. In addition, exposure to toxic substances, including smoking, alcohol, radiation or environmental pollutants also leads to

oxidative stress. Since it is believed that a high level of reactive oxygen species leads to infertility, an obvious and logical solution to this condition is the assumption that increased consumption of antioxidants will not only help treat male infertility, but also prevent its occurrence. With the increasing recognition of the role of oxidative stress in the pathophysiology of male infertility, the role of antioxidants as one of the options for the treatment of idiopathic male infertility has also increased, while many oral antioxidant preparations are readily available on the market. In comparison with the use of hormonal drugs and assisted reproductive technologies, antioxidants are relatively safe, inexpensive and widely available, and the growing volume of clinical research data in urology confirms their effectiveness in improving ejaculate parameters and live birth rates. However, the treatment of oxidative stress should primarily include strategies to reduce or eliminate stressful conditions: smoking, obesity, alcohol, physical inactivity, varicocele, infections of the reproductive system, gonadotoxins and hyperthermia.

The link between obesity and male infertility is probably multifactorial. Spermatogenesis is regulated by the interaction between the hypothalamus, pituitary gland and testicles. The initial link in the regulation of spermatogenesis is the anterior lobe of the hypothalamus, in which gonadotropin-releasing hormone (GnRH) is synthesized, which has a regulating effect on the pituitary gland, in the anterior lobe of which hormones are synthesized that directly regulate the work of testicular tissue: follicle-stimulating hormone (FSH) and luteinizing hormone (LH). In the testicular tissue, follicle-stimulating hormone regulates the work of the spermatogenic epithelium, which synthesizes proteins involved in spermatogenesis, transport and maturation of sperm, as well as homeostasis of seminal plasma. On the other hand, LH acts on glandulocytes, stimulating the production of testosterone. In obese men, compared with men without excess adipose tissue, a lower level of serum testosterone is more often detected. Excess adipose tissue also leads to an increase in the conversion of testosterone to estradiol, which can lead to secondary hypogonadism through suppression of the hypothalamic-pituitary-gonadal axis. In addition, estrogens negatively regulate the secretion of gonadotropin-releasing hormone, luteinizing hormone and follicle-stimulating hormone, which determine the functional connections between the brain and testicles.

Due to the fact that the foods we consume are complex multi-component objects, the traditional approach to assessing the relationship between the consumed foods and the disease, which focuses on the effects of nutrients individually, may not be sufficient to take into account the cumulative relationships and synergistic effects on bioavailability, circulation levels, metabolism and excretion of nutrients.

The data obtained in a number of studies have shown a decrease in the process of fibrosis of prostate tissue against the background of the inflammatory process when using collagenases [7]. One of the possible drugs that can be considered as a means of reducing fibrosis is the enzyme bovgialuronidase azoximer – a complex drug with enzymatic (hyaluronidase) activity of prolonged action. The effectiveness of this drug is associated with the ability to reduce

inflammatory tissue edema, «depolymerize the matrix of connective tissue in fibrous granulomatous formations, as well as the suppression of the reverse regulatory reaction aimed at the synthesis of connective tissue components».

The problem of the male factor of infertile marriage is a significant medical and social factor. Polyethologicity of this condition determines the complexity of effective curation. In a situation where it is impossible to single out one or more causal factors unambiguously, the syndromic approach, expressed in the appointment of antioxidants, has now become widespread. However, with a consensus opinion on the effectiveness of such treatment, there remains a wide discussion on a specific range of active substances, their combinations, optimal timing and doses of administration.

We offer the following recommendations:

1. When examining patients with male infertility, it is advisable to conduct preliminary preparation with rectal suppositories of azoximer bovgialuronidase 3000 IU every other day No. 5 in order to increase the effectiveness of detecting microorganisms during bacteriological examination of the ejaculate.
2. If an idiopathic nature of disorders is suspected in men with infertility, it is advisable to determine the levels of vitamins C, E and trace elements selenium and zinc in order to identify deficient conditions critically important for the realization of reproductive function with the aim of subsequent correction with monocomponent drugs in the maximum permitted daily dosages.

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