FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL (ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

Journal Website: https://frontlinejournals.org/journals/index.php/fmspj

Research Article

PROBLEMS OF OPTIMIZING TREATMENT OF INFERTILITY IN PATIENTS WITH VARICOCELE

Submission Date: January 20, 2023, **Accepted Date:** January 25, 2023,
Published Date: January 30, 2023
Crossref doi: https://doi.org/10.37547/medical-fmspj-03-01-02

Furkatov Akbarshoh
Urologist-Andrologist Of The Surgical Department Of The Central Clinical Hospital Of The State Joint-Stock Company "Uzbekistan Temir Yollari", Uzbekistan

ABSTRACT

It is known that infertility of a couple is often associated with spermatogenesis disorders. The most common causes of male infertility are varicocele, inflammatory diseases of the reproductive system, hormonal disorders and cryptorchidism. Also, in many cases, it is difficult to determine the cause of male infertility. To date, there are no generally recognized methods of drug treatment of the idiopathic form of male infertility, and its therapy is often considered to be of an empirical nature. Assisted reproductive technologies are highly effective methods of infertility treatment, but they are expensive and invasive.

KEYWORDS

Varicocele, spermogram, male infertility, therapy, assisted reproductive technologies.

INTRODUCTION

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

Infertility, as a rule, is understood as the inability of a couple to get pregnant after regular (at least 3 times a month) unprotected sex for a year. The payback of this pathology is about 15%. Let us dwell on some of the characteristics of infertility, which directly follows from the above definition. First of all, infertility is a clinical diagnosis. It will not be possible to determine it only on the basis of any laboratory data indicating the possible cause of infertility.

Secondly, this disease affects the couple, and one or even both couples can have children with another person. According to available statistics, in about 20% of cases, infertility occurs only in men, 50% - only in women, and in the remaining 30%, there is a disorder in both. Thus, the violation of spermatogenesis plays an important role in at least half of cases of infertility.

Thirdly, the term" infertility " itself is not very correct, since it literally means that getting pregnant is a complete failure, in most cases it is only about reducing its likelihood. In this regard, other terms such as “subfertility” and “decreased fertility” have been proposed to designate the problem under discussion, although they have not yet been widely used [1].

In general, it should be remembered that judgments about the fertility or the ability to conceive a particular patient are of a very approximate nature, which mainly determines the methods of treatment of patients, which we will discuss below. The above statistics allow us to imagine the scale of the problem of male infertility. This determines the relevance of this issue not only for urologists, but also for health care and society as a whole. In most literature, it is customary to divide male infertility into secretory and excretory (obstructive) [2].

In our opinion, it is justified to distinguish the last group, because the term "secretory infertility" will not be very accurate due to the large number of possible causes of such a disorder. It should also be noted that in at least 25% of cases of male infertility, modern examination methods do not allow us to determine the causes of the disorder [3]. Such patients are diagnosed with idiopathic infertility. We can assume that this form of fertility disorder is the result of the complex effects of negative environmental factors, as well as currently unknown diseases.

THE MAIN PART

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

Among the identified causes of male infertility, the most common is varicocele - dilation of the veins of the pampiniform plexus of the spermatic cord. Despite the fact that the ability of varicocele to cause male infertility has long been known, there is still a lot of uncertainty about this issue. In particular, it is known that varicocele is widespread and occurs in a significant proportion (8–13%) of men without spermatogenesis disorders, although its frequency is significantly higher in male infertility (25–40%). It is assumed that additional factors are necessary for the development of spermatogenesis disorders as a result of varicocele; in addition, it is possible that there are various forms of this disease.

And the mechanisms that cause fertility disorders in patients with varicocele have not yet been definitively clarified, while changes in temperature and hemodynamics in testicular tissue are currently of the greatest importance. hence, the role of infectious agents in the development of male infertility continues to be controversial. The fact that viral orchitis and tuberculous epididymitis can lead to infertility is beyond doubt. However, the significance of other infections has not been definitively established. In particular, today it cannot be unequivocally stated that Ureaplasma urealyticum, Chlamydia trachomatis and other pathogens of infections of the male reproductive system have a negative impact on fertility [4].

The significance of cryptorchidism in the development of male infertility is beyond doubt. Its frequency in the anamnesis of men suffering from infertility significantly exceeds that in the general population (9.4 and 2.4%, respectively). The proportion of genetic disorders among the causes of MB development is relatively small, but among men with a complete absence of spermatozoa in the ejaculate (azoospermia), they are quite common (up to 20% of cases). Often, azoospermia is also caused by obstruction of the genital tract (excretory infertility) and severe hormonal disorders. The pathogenesis of male infertility is not well understood.

To date, various, including unknown (idiopathic) etiological factors usually trigger similar pathogenetic processes, the final result of which is a decrease in the number and / or quality of spermatozoa [5]. An exception is some forms of male infertility characterized by a specific pathogenesis, in particular, excretory disorders that make it difficult to transport spermatozoa through the genital tract, as well as serious

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

hormonal changes characterized by a sharp loss of spermatogenesis. Oxidative stress is currently considered one of the most important pathogenetic mechanisms of the development of male infertility. Its cause is an abnormal accumulation of molecules containing oxygen in an unrecoverable form – the so-called reactive oxygen species (ROS; reactive oxygen species).

Normally, the formation of ROS is balanced by the action of various antioxidant systems, however, in pathology, there is an excess of ROS in the testicular tissue, affecting spermatogenesis cells sensitive to oxidative stress. The most active synthesis of ROS occurs in leukocytes and immature gametes, which explains the importance of oxidative stress in the development of infertility in inflammatory diseases of the male reproductive system, varicocele and hormonal disorders confirmed by a number of studies [6].

The antioxidant system of the seminal tubules includes enzymes (superoxide dismutase, catalase, glutathione peroxidase), small molecules (tocopherols, carotenes, ascorbic acid) and chelating proteins (trans-, lactoferrin, ceruloplasmin). With the development of imbalance and increased oxidative stress, ROS, out of control of the antioxidant system, damage various structures of spermatogenesis cells, including DNA, membranes and various intracellular proteins. The result of this process in the testicles is damage to the spermatozoa, leading to their death, violations of the structure and / or functional qualities (mobility and ability to fertilize).

Another important pathogenetic mechanism for the development of male infertility is an increase in the apoptosis process, that is, programmed cell destruction. Typically, pro-and anti-apoptotic factors are in equilibrium, which are disrupted by the etiological factors discussed above. An increase in apoptosis in testicular tissue has been detected in various forms of male infertility, including varicocele, inflammatory processes, and hormonal disorders [7].

so, despite the continuation of some contradictions, at present, surgical intervention, primarily venous microsurgery, is a typical method of treating spermatogenesis disorders in patients with varicocele. As mentioned above, in most cases it will not be possible to determine the cause of male infertility. In addition, etiotropic treatment does not help many patients (first of all, this applies to patients with varicocele). In such

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

cases, empirical treatment is prescribed, aimed at correcting the pathogenetic mechanisms of spermatogenesis disorders, which, as mentioned above, are common for most forms of infertility.

Before proceeding to the description of various methods of empirical or pathogenetic therapy, it is necessary to dwell on the methodological features of studying the effectiveness of these methods in the treatment of male infertility. First, in the absence of treatment, the frequency of pregnancy in couples suffering from infertility caused by impaired spermatogenesis is about 1% per month, and when observed for 3 years, it reaches 26% [8].

Thus, in many cases it is difficult to judge whether conception is related to the treatment. Secondly, taking into account the data presented above about the insufficient relationship between the spermogram indicators and the probability of conception, the results of many studies in which the effectiveness of drugs was evaluated by the dynamics of changes in the spermogram are currently being questioned. Often these results are not confirmed by works in which the effectiveness is evaluated by the frequency of pregnancies. Hormone therapy occupies a prominent place among the methods of empirical treatment of male infertility. It is well known that androgens, primarily testosterone, play an important role in the formation of the male reproductive system and secondary sexual characteristics.

At the same time, the role of testosterone in spermatogenesis seems to be quite complex, and when administered in large doses, it suppresses the synthesis of spermatozoa by inhibiting the release of luteinizing and follicle-stimulating by the mechanism of negative feedback. In the past, attempts have been made to use testosterone in the treatment of male infertility, but placebo-controlled studies have shown that such treatment not only does not increase the likelihood of conception, but often worsens the indicators of spermatogenesis [9].

The most justified from a pathogenetic point of view is the use of gonadotropins in male infertility, that is, substances with the qualities of follicle-stimulating and/ or luteinizing. However, despite the fact that a number of previous studies have shown an improvement in spermogram indicators and even an increase in the frequency of conception against the background of the administration of gonadotropins, these effects

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

have not been confirmed in placebo-controlled studies [10].

None of the drugs, including chorionic gonadotropin, menopausal gonadotropin and recombinant luteinizing and follicle-stimulating, provided a statistically significant increase in the probability of conception. Recall that in this case we are talking about the use of these drugs in men without obvious hormonal disorders, in the presence of which they are naturally highly effective. A similar situation also exists with respect to other drugs widely used in clinical practice for the treatment of male infertility – the antiestrogens clomiphene and tamoxifen. Their positive effect on spermogram parameters and pregnancy rate shown in a number of uncontrolled studies has not been confirmed in placebo-controlled studies [11].

Another group of widely used antioxidant agents are vitamins. Vitamin E is the most widely used in the treatment of male infertility in clinical practice. Indeed, according to a number of studies, taking this vitamin made it possible to improve many spermogram indicators, primarily sperm motility. Unfortunately, these effects have not been confirmed in placebo-controlled studies. So, Rolf S. et al. A double-blind study was conducted in which the efficacy of oral vitamin E intake was studied in patients with asthenozoospermia [12]. The patients received the drug for 56 days, after which the authors found no statistically significant changes in the parameters of the spermogram or the facts of conception. It should be noted that the duration of the observation period in this study could not be sufficient to achieve the effect, because it was inferior to the duration of the sperm development cycle.

Significant interest in recent years has been caused by the use of trace elements with antioxidant properties in the treatment of male infertility, however, in our opinion, this topic deserves consideration in a separate article. Attempts have also been made to treat male infertility using coenzyme Q10 and carnitine. Interestingly, the latter drug in two placebo-controlled studies demonstrated efficacy in relation to sperm motility, but the frequency of conception did not change. Nevertheless, carnitine is currently considered one of the most promising drugs for the treatment of male infertility. The effect of drugs from the group of α-blockers on spermatogenesis has been studied in several works. However, although their use led to

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

an increase in the concentration of spermatozoa, other spermogram indicators, as well as the number of conceptions among those receiving the drug, did not exceed those in the control group [13].

CONCLUSIONS

The use of assisted reproductive technologies is the most effective method of treating male infertility today. Assisted reproductive technologies include:

- Intracytoplasmic sperm injection (ICSI) – a separate sperm is placed in the cytoplasm of a mature egg; • partial zone separation (PZD) – in two places, the integrity of the shiny shell (zona pellucida) is violated using a pointed glass pipette; through these ruptures, spermatozoa penetrate into the egg;
- subzonal sperm injection (SUZI) – selected spermatozoa are injected using a glass pipette into the perivitelline space (perivitelline space).

However, the use of assisted reproductive technologies is limited by high cost and invasiveness. In addition, to date, the indications for their use have not been determined and in practice, in each case, the decision is made individually. There are situations in which the expediency of assisted reproductive technologies is beyond doubt, for example, in excretory infertility, when spermatozoa are obtained surgically. At the same time, in idiopathic infertility, the severity of assisted reproductive technologies should be compared with the probability of success with other approaches. It is also necessary to take into account the state of the partner's reproductive health. The most effective is the intracytoplasmic injection of sperm, which allows to achieve implantation in about 60-65% of cases with the use of ejaculate and in 50-60% – with the use of sperm obtained surgically. The frequency of pregnancies carried out is about 33%, which is associated with a higher probability of spontaneous abortions and congenital anomalies compared to normal conception [14].

So, unfortunately, we have to state that the effectiveness of most drugs currently used for the treatment of male infertility has not been proven. This, of course, makes it difficult to choose an adequate method of treatment, more precisely, indications for the use of assisted reproductive technologies in patients with infertility and a

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

relatively average deviation in the spermogram. On the other hand, we must not forget that in such patients, even without treatment, conception is very likely to occur. Unfortunately, there are practically no clear criteria for choosing one or another method of treating male infertility, which determines the need for many future studies in this direction.

It is also necessary to inform subfertile men with clinical varicocele. Because, even when varicocele is the only identified cause of infertility, that the age is older than 31 years, the duration of infertility is more than 38 months, as well as the initially low numbers of progressively mobile sperm in the ejaculate (less than 15 million) are predictors of low efficiency of varicocele correction and a high probability of using assisted reproductive technology protocols. The criterion of "clinically significant improvement", that is, an increase in the number of progressively mobile spermatozoa in the ejaculate by 12.5 million and an algorithm for calculating the probability of natural conception can help in the clinical practice of a urologist, andrologist and proctologist in deciding on the further management of an infertile couple after analyzing the results of varicocele correction already 3-6 months after surgery.

REFERENCES

1. Macomber D., Sanders M. The spermatozoa count: its value in the diagnosis, prognosis and concentration in fertile and infertile men // N Engl J Med. 1999. Vol. 200. – P. 981-984.
2. Alyaev Yu.G., Chaly M.E., Grigoryan V.A. Disorders of reproductive function in men. Practical guide. – M., 2016.
3. Tanevsky V.E. Comparative analysis of the effectiveness of varicoceleectomy in sub(in-)fertile patients // Andrology and genital surgery. 2011. No. 1. – pp. 25-39.
4. Lopatkin N.A., Morozov A.V., Dzeranov N.K. Transfemoral endovascular obliteration of the testicular vein in the treatment of varicocele // Urology and nephrology. 1993. Issue 6. – pp. 50-53.
5. Ying H.Q., Qi Y. Association of GSTM1 and GSTT1 genes with the susceptibility to male infertility: result from a meta-analysis // Genet Test Mol Biomarkers.

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL (ISSN – 2752-6712)
VOLUME 03 ISSUE 01 Pages: 12-20
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605)
OCLC – 1272874727
Publisher: Frontline Journals

2013 Jul. Vol.17 (7). P. 535-542. Epub 2018 Apr 30.

6. Tirumala Vani G., Mukesh N. Role of glutathione S-transferase Mu-1 (GSTM1) polymorphism in oligospermic infertile males // Andrologia. 2018 Aug. Vol. 42 (4). – P. 213–217.
7. Rossitto M., Rigoli L., Procopio V., Ciccolo A. The role of the incidence of genetic abnormalities on the onset and on the results of the surgical repair of varicocele // Ann Ital Chir. 2018 May-Jun. Vol. 81 (3). – P. 161.
8. Strakhov S.N. Dilatation of the veins of the spermatic cord: Lecture "Problems of diagnosis and treatment of varicocele". – M., 2015.
9. Teodorovich O.V., Kadyrov 3.V., Alkhasov G.M. Hemodynamics of the scrotum organs in patients with bilateral varicocele // Andrology and genital surgery. – No. 1. – M., 2017.
10. Kondakov V.T., Pykov M.I. Varicocele. – M.: Vidar-M, 2020.
11. Rolf C., Cooper T.G., Yeung C.H. and Nieschlag E. Antioxidant treatment of patients with asthenozoospermia or moderate oligoasthenozoospermia with high-dose vitamin C and vitamin E: a randomized, placebo-controlled, double-blind study. 2019.
12. Kadyrov Z.A. Laparoscopic urological surgery // Urol. and nephrol. – Minsk, 2019.
13. Gritsulyak B.V., Zebra N.P. Influence of varicocele on spermatogenesis and interstitial endocrinocytes /B.V.Gritsulyak, N.P.Zbirak //Morphology. – Kiev, 2019.
14. Erokhin A.P. Varicocele as a cause of infertility // Andrology and genital surgery. – M., 2016.