



TREATMENT OF SPERMATOLOGIC DISORDERS AND OXIDATIVE STRESS AFTER REPRODUCTIVELY SIGNIFICANT DISEASES CAUSED BY SEXUALLY TRANSMITTED INFECTION

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This study evaluated the efficacy and safety of two organic dietary supplements, AndroDoz and Testogenon, in the treatment of 58 men with spermatologic disorders and oxidative stress after experiencing reproductively significant diseases caused by sexually transmitted infection. Over a 12 week period, 38 patients (test group) received both AndroDoz and Testogenon as a combination therapy, whereas 20 patients (control group) received AndroDoz alone. The combination therapy with both AndroDoz and Testogenon showed a statistically significant increase in treatment effectiveness. A positive clinical effect was noted in 92.2% of patients in the test group who received combination therapy. This was reflected as an increased concentration and mobility level of spermatozoa, similar to values observed in men with normozoospermia. Moreover, these men exhibited a two-fold reduction in the risk of fertility disorders due to DNA fragmentation in spermatozoa; their testosterone also increased to normal levels. Additionally, patients in the test group showed improvement in the quality of erection and increased blood flow in the prostate gland and testicles. Men in the control group, who received monotherapy with AndroDoz, did not show improvement similar to that of men in the test group; normozoospermia was established in 70% of men in the control group. These results confirm that AndroDoz and Testogenon are more effective when used concomitantly. These supplements showed no side effects and could be used in complex treatment of spermatologic disorders and oxidative stress in men who experienced reproductively significant diseases caused by sexually transmitted infection.

⊗ **Keywords:** reproductive health; sexually transmitted diseases; spermatogenesis; oxidative stress; AndroDoz; Testogenon.

ЛЕЧЕНИЕ СПЕРМАТОЛОГИЧЕСКИХ НАРУШЕНИЙ И ОКСИДАТИВНОГО СТРЕССА ПОСЛЕ ПЕРЕНЕСЕННЫХ РЕПРОДУКТИВНО ЗНАЧИМЫХ ЗАБОЛЕВАНИЙ, ВЫЗВАННЫХ ИНФЕКЦИЯМИ, ПЕРЕДАЮЩИМИСЯ ПОЛОВЫМ ПУТЕМ

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⊗ Проведено исследование эффективности и безопасности натурального комплекса многокомпонентных биологически активных добавок АндроДоз и Тестогенон при лечении 58 мужчин со сперматологическими нарушениями и оксидативным стрессом после перенесенных репродуктивно значимых заболеваний, вызванных инфекцией, передающейся половым путем. В течение 12 недель 38 больным основной

группы назначали комбинированную терапию Андродозом в сочетании с Тестогеноном, 20 пациентов контрольной группы получали только Андродоз. Установлено, что назначение комбинированной терапии компонентов комплекса Андродоз и Тестогенон статистически значительно повышает эффективность лечения. Положительный клинический эффект отмечен у 92,2 % больных основной группы, получавших комбинированную терапию. Это выражалось в увеличении концентрации и подвижности сперматозоидов до нормозооспермии, снижении в два раза риска нарушения фертильности по фрагментации ДНК в сперматозоидах, повышении уровня тестостерона до нормальных значений, улучшении качества эрекции, усилении кровотока в предстательной железе и яичках. В контрольной группе, в которой проводили монотерапию Андродозом, эффект был несколько меньшим — нормозооспермия была достигнута у 70 % пациентов. Полученные результаты подтверждают, что компоненты комплексов Андродоз и Тестогенон в комбинированной терапии эффективны, безопасны, не имеют побочных эффектов и могут применяться в комплексном лечении сперматологических нарушений и оксидативного стресса у мужчин после перенесенных репродуктивно значимых заболеваний, обусловленных инфекцией, передающейся половым путем.

🔑 **Ключевые слова:** репродуктивное здоровье; заболевания, передающиеся половым путем; сперматогенез; оксидативный стресс; Андродоз; Тестогенон.

INTRODUCTION

Reproductive health is a crucial part of the general health of every family and society. Reproductive health is defined as a state of complete physical, mental, and social well-being including the ability to have sexual relations without risk of contracting sexually transmitted diseases, safe during pregnancy, childbirth, survival, and health of infant, maternal welfare, and plan future pregnancies, including prevention of undesirable pregnancy.

The insufficient support of the reproductive health of fertile-aged men is a current topical issue in public health service. Routine and consistent follow-up examination of the reproductive health of men aged 18 years and older is lacking. Furthermore, among adolescents aged 15–17 years, the incidence rate of reproductive and urogenital disorders caused by sexually transmitted infections (STIs) due to early and frequently unprotected sexual activity due to early sexual activity and frequently without protection is increasing [1–5]. These disorders are socially significant diseases that are most commonly spread by sexual intercourse. The main STIs, of which there are more than 30 types, include *Chlamydia*, *Mycoplasma*, *Ureaplasma*, trichomoniasis, human papillomavirus, herpes, gardnerellosis, gonorrhea, syphilis, and human immunodeficiency virus/acquired immunodeficiency syndrome. They compromise male and female reproductive health and urogenital system, increase the risk for congenital pathology in children, and negatively affect demography and economy [6]. STIs differ from other human diseases by etiology, epide-

miology, pathogenesis, treatment, and prophylaxis. The incidence of STIs increases with the prevalence of *Chlamydia*, which infects more than 90 million people in Europe and more than 1 billion people worldwide. Awareness of STIs is important given its high incidence and high risk of complications, including infertility [7–12].

STIs are strongly associated with inflammatory diseases of male organs relevant for reproduction. These organs include the main sex glands, or the gonads (testicles), and accessory organs, namely, prostate gland, seminal vesicles, and epididymides, which are enzyme-secretory-hormone-driven glands producing citric acid, spermine, fructose, and carnitine that influence sexual function. In the recent two decades, the incidence rate of chronic prostatitis has increased. Almost one-third of patients with chronic prostatitis have sexual disorders such as premature ejaculation and erectile dysfunction. A great social hygienic importance is also referred to chronic epididymitis, as its development in sexually active men younger than 35 years is more often associated with *Chlamydia*. Thus, *Chlamydia* infection is diagnosed in 57% of patients with chronic epididymitis, whereas gonococci in 17%, *Ureaplasma* and *Mycoplasma* in 13% of patients, and acute epididymitis *Chlamydia* are identified only in 2% of patients [13, 14]. In men over 35 years old, epididymitis is more frequently associated with non-STIs of the urinary tract. Male infertility was shown to be due to urogenital infections in 20% of cases, where atypical intracellular microorganisms (*Chlamydia*, *Mycoplasma*, and *Ureaplasma*)

negatively affected sperms, impairing their function and inducing apoptosis. In patients with chronic non-bacterial prostatitis (category IIIB) or chronic pelvic pain syndrome, atypical microorganisms (*Chlamydia*, *Trichomonas*, *Mycoplasma*, and *Ureaplasma*) were found in the prostatic fluid even without an increase in the number white blood cells, and *Chlamydia* infects 62% and *Ureaplasma* infects 13% of these patients; for those with chronic prostatitis of category IIIA with increased white blood cells in the prostatic fluid, only 26% of the patients had three times less *Chlamydia*. Decreased levels of the immune cellular and humoral markers were proved in patients with chronic prostatitis associated with *Chlamydia*, *Mycoplasma*, and *Ureaplasma* [15–18]. These microorganisms enter into the cell space, reach the pelvic lymph nodes, infect the peripheral blood lymphocytes, are absorbed in epithelial membranes and sperms, and spread into the prostatic fluid, increasing the level of anti-sperm antibodies in the ejaculate and serum, which declines after eradication of the causative agent. STI-associated inflammatory diseases of the male genital organs (prostatitis and epididymitis) may cause non-obstructive and obstructive azoospermia and infertility, in which long-term treatment, sometimes assisted reproductive technologies, and surgery are necessary [19–21].

An STI-associated chronic inflammation in the prostate gland in 30%–50% of patients leads to a decrease in the level of macrophage nitric oxide (NO), causing damage to epithelial cell wall and DNA of the prostate gland. NO is synthesized mainly from the amino acid arginine with the participation of the enzyme NO synthase (NOS) in three isoforms, namely, macrophage, neuronal, and endothelial isoforms. Neuronal and endothelial isoforms facilitate NO synthesis under normal conditions, regulating the activity of the nervous and vascular systems, and macrophage NOS is normally not active and is stimulated by various pathogenic factors. NO deficiency leads to prostatic ischemia, which contributes to the development of an anaerobic infection in the prostate gland not detectable by usual laboratory methods. Notably, the detection rate of venous prostatic discirculation increases with age in proportion to the decrease in total testosterone [22, 23].

Recently, the role of oxidative stress in the formation of male infertility garnered considerable attention. Oxidative stress is caused by hyperproduction of reactive oxygen species. Oxidative stress causes

damage to the DNA of chromosomes and sperm membrane, initiates their apoptosis, leads to a decrease in the concentration and mobility of sperm cells, impairs their fertilizing ability, and causes oxidative damage to cellular lipids, proteins, and DNA [23–26].

As the leading hormone, testosterone plays the main role in the development of the male genital glands (testicles and prostate) and the formation of secondary sexual characteristics, sexual desire, and spermatogenesis. At age 30–35 years, testosterone synthesis in men gradually decreases at 1%–2% per year. Testosterone production is controlled by the hypothalamus–pituitary–gonadal system. The releasing hormone is released from the hypothalamus, stimulating the production of luteinizing (LH) and follicle-stimulating hormones (FSH). LH stimulates testosterone synthesis by Leydig cells and promotes testicular development. FSH and testosterone regulate spermatogenesis. In testosterone deficiency syndrome, dysregulation occurs in the hypothalamus–pituitary system, and a decrease in the number of Leydig cells is associated with impaired blood circulation in the testicular tissues and a decrease in the number of LH receptors on their surface [27, 28].

Currently, the issue of the diagnosis and treatment of reproductive disorders in men with an STI remains relevant and understudied. Therefore, in the present study, we investigated the efficacy of using multicomponent natural complexes AndroDoz (Stada, Germany) and Testogenon (LLC “VIS,” Russia) belonging to a group of dietary supplements in such patients. These drugs can compensate for the lack of antioxidants, minerals, and vitamins in patients with sperm and reproductive disorders and a history of STIs, improve and restore spermatogenesis, increase testosterone production, and improve the blood supply to the scrotum and prostate gland [29].

The preparation of AndroDoz includes a balanced complex for improving spermatogenesis and had nine components: L-arginine, L-carnosine, L-carnitine, coenzyme Q, glycyrrhizic acid, zinc, selenium, and vitamins E and A.

L-arginine is a conditionally essential amino acid and a necessary precursor for syntheses of proteins and many biologically important molecules. It is a substrate for the synthesis of NO using the enzyme NOS. It increases the production and quality of sperm, has a beneficial effect on the function of the prostate

gland, and normalizes blood flow in the pelvic organs. L-arginine increases blood oxygen saturation and enhances the fertilizing function of the semen.

L-carnosine is a natural component of human tissues and a powerful water-soluble antioxidant. It enhances the effect of fat-soluble antioxidant α -tocopherol.

L-carnitine is a natural vitamin-like substance that participates in the processes of maturation of sperm, directly affects the male reproductive capacity, and increases the number and motility of sperm. L-carnitine aids in the maturation of sperm cells and stabilizes their membranes and fertilizing ability. Since sperm maturation lasts 74 days, it is very important not to interrupt the intake of L-carnitine and other substances important for this process throughout this time.

Coenzyme Q is the most important element of the synthesis of biochemical energy carriers. It is a powerful antioxidant capable of restoring the antioxidant activity of vitamin E. It has proven synergy with L-carnitine, which contributes to an increase production of spermatozoa and an improvement in their mobility.

Glycyrrhizic acid inhibits the activity of the component of the coagulation system –thrombin—including those present in the semen and participating in the process of sperm thickening. This substance stimulates the secretion of the hormone secretin, contributing to the dilution of secretions of various glands.

Selenium is a chemical element whose deficiency can lead to a decrease in sperm production and infertility in men. This is a powerful antioxidant that inhibits lipid oxidation and protects cells from the destructive effects of free radicals, which damage cell membranes and the genetic material of the sperm cell. Selenium is necessary not only to increase the number of sperm but also to release testosterone. When used in combination with vitamin E, the action of selenium is enhanced. In the experiment, selenium can protect spermatogenesis from acute and chronic intoxications. Selenium has a pronounced synergistic effect with vitamins A and E and reduces their decomposition while reducing the body's need for these vitamins.

Zinc plays an important role as it is a component of several hundred enzymes in the human body, including those involved in the polymerization of DNA and RNA. Zinc deficiency causes changes in chromo-

somes, leading to infertility. Zinc is also needed in the production of sex hormones. This microelement is contained in the semen in a very high concentration.

Vitamin E (tocopherol) is a potent antioxidant and improves the quality of sperm by stabilizing the synthesis of hormones. It is the sex hormone that provides the genitals with oxygen, as its name means "bearing progeny." Tocopherol has a positive effect on the ability of the sperm to penetrate the egg. It participates in the proper uptake and metabolism of carnitine.

Vitamin A directly affects the production of sperm, increases sperm motility, prevents their agglutination, and increases their fertilizing ability. Vitamin A participates in the uptake and metabolism of carnitine.

The complex Testogenon includes 10 components. Yohimbe bark extract enhances erection with a simultaneous increase in blood flow to the cavernous body of the penis. At the same time, it affects the cerebral cortex and subcortical centers, thereby removing the feeling of insecurity, stiffness, and fear. It helps increase libido and the duration of erection, enhancing sexual and emotional sensations during intimacy. Pygeum bark extract reduces blood stasis, decreases edema and inflammation of the prostate gland, prevents excessive synthesis of fibroblasts, stops prostate hyperplasia, helps prevent the formation of tumor tissue, improves the urinary system function, increases the elasticity of the bladder, reduces urinary frequency, facilitates urination, prevents urogenital infection, helps establish hormonal balance, and normalizes reproductive system activity. The extract of wild yam roots has adaptogenic properties and improves microcirculation in the reproductive organs. Ginseng root extract improves the functions of the prostate gland function and sexual activities, and it has tonic, restorative, and stimulating properties. The active ingredients of ginseng actively affect the central nervous system, increase productivity, reduce physical and mental fatigue, improve appetite, and stimulate sexual function. In addition, ginseng improves cardiovascular function and regulates blood pressure level. Vitamin B₆ has a positive effect on the function of the cardiovascular, endocrine, and immune systems. It also strengthens the energy potential of sperm, which is important in case of their reduced mobility. Vitamin B₅ is involved in testosterone synthesis and needed to in-

crease life expectancy. It plays an important role in carbohydrate and fat metabolism and synthesis of certain hormones. It has a regulating effect on the nervous system and intestinal motility. Vitamin B₁₂ is one of the substances necessary for the health of the male reproductive organs. Indeed, it can control the sperm content in the seminal fluid. This vitamin participates in cell division; thus, tissue synthesis is impossible without it. It plays an important role in the production of methionine. Vitamin C is necessary for the normal functioning of the genitals. It improves the body's resistance to harmful environmental factors. It is a powerful antioxidant. Vitamin C is essential for the formation of hormones and production of adrenaline. It helps the human body cope with the effects of stress and increases the body's resistance. Testogenon also includes the above-described amino acid L-arginine and vitamin E (tocopherol). Experimental studies showed that the use of Testogenon in doses that maximally exceeded the daily requirement for a person was harmless and safe, and an analysis of Testogenon's specific activity established its stimulating effect on the production of endogenous testosterone [28, 29].

The aim of this study was to investigate the efficacy and safety of AndroDoz and Testogenon for the treatment of sperm disorders in men with a history of STIs.

MATERIAL AND METHODS

Diagnostic findings of 58 men aged 20–40 years (mean age, 30 years) with reproductive and sperm disorders and a history of STI were analyzed. Patients were followed in the consulting and diagnostic center of a urology clinic in North-Western State Medical University named after I.I. Mechnikov based in Alexandrovskaya Hospital and in city polyclinics of St. Petersburg during the period from September 2017 to December 2017.

Observed patients complained of a decline in semen analysis parameters and weakening of spontaneous and adequate erections. All patients were previously treated in various medical institutions for chronic prostatitis; chronic epididymitis caused by *Chlamydia*, *Mycoplasma*, and *Ureaplasma*; and urogenital infection. The patients were divided into two groups, namely, study group and control group. The study group included 38 patients who had testosterone levels at the lower limit of normal. These patients received combined treatment with AndroDoz two

capsules twice a day for 12 weeks and Testogenon one capsule once a day for 4 weeks. The control group included 20 patients with normal testosterone levels who received AndroDoz also two capsules twice a day for 12 weeks.

The inclusion criteria for the study were age 20–40 years, presence of changes in the semen analysis, laboratory evidence of partial androgen deficiency (levels of total testosterone 8–12 nmol/L), a moderate decrease in erectile function, absence of STIs according to bacterioscopic and bacteriological studies of scrapings from the urethra, prostate secretion or post-massage urine and ejaculate, absence of leukocytospermia, and elevated leukocyte count in the prostatic fluid. The exclusion criteria were testosterone levels <8 nmol/L, hyperprolactinemia, acute inflammatory diseases of the genital organs, chronic bacterial prostatitis, prostate stones, obstructive azoospermia, urethral strictures, elevated PSA levels >4 ng/mL, diabetes, varicocele, and mental diseases.

Before enrollment in the study, each patient signed an informed consent form. In all patients, clinical urine analysis and clinical and biochemical blood tests were performed, and their levels of sex and gonadotropic hormones, prostate-specific antigen in the blood serum, and antisperm antibodies (ASA) in the ejaculate and serum were measured. DNA fragmentation in the spermatozoa was performed on a FACSCantoll flow cytometer using monoclonal antibodies manufactured by Roche. All patients underwent digital rectal examination of the prostate gland, transrectal ultrasonography with prostate Doppler ultrasonography, and scrotal Doppler ultrasonography. The ejaculate was examined using Makler counting chambers in accordance with the WHO requirement [27]. Microscopy of the prostatic fluid was performed on a binocular microscope at a magnification of 400 times. Erectile function was evaluated on the basis of the International Index of Erectile Function. Examinations were performed prior to treatment, after 4 weeks of treatment, and after 12 weeks of treatment.

The results were processed by conventional statistical methods with the calculation of the average value, and the confidence interval was at a confidence level $\alpha = 0.95$ (error probability $p < 0.05$). Statistical data analysis was performed using the application statistics software package SPSS 12.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Positive dynamics in semen analysis parameters was observed in two groups in the course of the treatment (Table 1). In the group of combined therapy with AndroDoz and Testogenon, the initial mean ejaculate volume was 2.1 ± 1.3 mL, 3.2 ± 1.1 mL after 4 weeks, and 4.1 ± 0.9 mL 12 weeks later, i. e., increased two times ($p < 0.05$ compared with values prior to treatment). In the group of AndroDoz only, the mean ejaculate volume prior to treatment was 2.3 ± 1.5 mL, after 4 weeks was 3.0 ± 1.2 mL, and 12 weeks after treatment was 3.3 ± 1.1 mL ($p < 0.05$ compared with values prior to treatment). Thus, statistically significant dynamics was noticed in two groups. Before treatment, both groups showed a decrease in concentration, mobility, and an increase in the number of morphologically modified forms of spermatozoa, which corresponded to oligoasthenoteratozoospermia (OAT syndrome). Sperm concentration increased in the two groups during the treatment course. In the study group, the mean sperm concentration before treatment was 13.8 ± 4.8 M/mL, after 4 weeks was 14.6 ± 4.2 M/mL, and after 12 weeks was 22.2 ± 3.9 M/mL. In the control group, the mean sperm concentration was 13.5 ± 5.9 , 14.4 ± 5.5 ,

and 15.1 ± 5.4 M/mL, respectively. After treatment, there was improvement in sperm motility in the two groups and slightly more prominent in the group of combined therapy. In the study group, the sperm motility before treatment was $25.8 \pm 9.1\%$, after 4 weeks was $30.3 \pm 8.6\%$, and after 12 weeks was $33.4 \pm 7.8\%$; in the control group, the sperm motility was $24.9 \pm 10.3\%$, $25.8 \pm 10.0\%$, and $30.5 \pm 9.7\%$, respectively. The decrease in the severity of sperm morphological defects occurred slightly faster in patients of the study group than in the control group. In the study group, initial values of this parameter exceeded the norm and amounted to $97.8 \pm 9.4\%$; after 4 weeks, it decreased to $75.1 \pm 13.1\%$, and 12 weeks after therapy cessation, it decreased to $58.7 \pm 19.4\%$. In the control group, the corresponding values were $84.4 \pm 12.2\%$, $78.3 \pm 15.4\%$, and $61.9 \pm 20.0\%$, respectively. The level of ASA before treatment in the study and control groups did not significantly exceed normal values. In the course of treatment, positive dynamics was noted regarding such an important indicator as DNA fragmentation in sperm cells. In the study group, the rate of 33.3% before treatment corresponded to high risk of infertility; after treatment, there was a two-fold decrease up to 15.1% ($p < 0.05$). Patients in the control group

Table 1

Changes in spermatological parameters over time in men in the test and control groups, $M \pm m$

Таблица 1

Динамика сперматологических показателей у больных основной и контрольной групп ($M \pm m$)

Criterion	WHO reference value, 2010	Study group ($n = 38$)			Control group ($n = 20$)		
		Before treatment	After 4 weeks	After 12 weeks	Before treatment	After 4 weeks	After 12 weeks
Sperm volume, mL	1.5 M/mL	2.1 ± 1.3	3.2 ± 1.1	$4.1 \pm 0.9^*$	2.3 ± 1.5	3.0 ± 1.2	3.3 ± 1.1
Sperm concentration, M/mL	1.5 M/mL	13.8 ± 4.8	14.6 ± 4.2	$22.2 \pm 3.9^*$	13.5 ± 5.9	14.4 ± 5.5	15.1 ± 5.4
Sperm motility	Grade A + B (<40) with progressive motility – 32%	25.8 ± 9.1	30.3 ± 8.6	33.4 ± 7.8	24.9 ± 10.3	25.8 ± 10.0	30.5 ± 9.7
Morphology	50% (58) > normal	97.8 ± 9.4	75.1 ± 13.1	$58.7 \pm 19.4^*$	84.4 ± 12.2	78.3 ± 15.4	61.9 ± 20.0

Note. $p < 0.05$ compared with pre-treatment values.

Примечание. $p < 0,05$ по сравнению с показателем до лечения.

had an average risk of infertility of 18.3% due to DNA fragmentation, which decreased to 16.3% after the treatment.

The dynamics in the level of sex and gonadotropic hormones in the observed patients was assessed before and after the 12 week course of treatment and compared with the normal values. However, the levels of FSH, LH, estradiol, and prolactin in patients of both groups were initially within normal values, but with a certain tendency to their increase, indicating a decrease in the production of the neuronal isoform of NOS in the hypothalamus–pituitary system. However, after 12 weeks of treatment, FSH and LH levels significantly decreased in both groups, but it was more pronounced in the study group (Table 2). The level of serum testosterone in both groups was initially at the lower limit of the normal, which was slightly lower in the study group. After 12 weeks, testosterone levels increased from 11.9 ± 5.8 nmol/L to 13.4 ± 5.6 nmol/L in the study group ($p < 0.05$) and from 12.8 ± 7.4 nmol/L to 12.9 ± 6.2 nmol/L. We speculated that the initial low testosterone level in patients with a history of diseases of accessory sex glands (prostatitis and epididymitis) was due to STIs and the toxic action of microorganisms on gonads, resulting in the decreased number and deformation of Leydig cells and appearance of LH receptors on their surface. In our patients, we explain that the reduction in spontaneous and adequate erection rate was due to not only a decrease in testosterone pro-

duction but also a decrease in the production of all NO isoforms (neuronal, macrophage, and endothelial), which in turn decreases the blood supply to the penis, prostate gland, and testicles. Combined therapy (AndroDoz + Testogenon) contributed to increased production of testosterone. In addition to serum testosterone in the study and control groups, we determined the normal level of sex hormone-binding globulin, or sex hormone. Metabolic syndrome was excluded, as this indicator may change dramatically. The digital rectal examination of the prostate gland in patients in both groups was painless and revealed minor areas of scarring and slightly reduced prostate volume. According to transrectal ultrasonography and Doppler ultrasonography before treatment, the prostate gland had a diffusely heterogeneous consistency with hyperechoic areas and reduced volume of $17\text{--}18\text{ cm}^3$ with some decline in blood flow rate in the subcapsular and paraurethral arteries to an average of 6.9 ± 3.8 cm/s in the study group and to 6.9 ± 4.1 cm/s in the control group (Table 3). After 12 weeks, the blood flow rate in the prostate gland increased to 9.8 ± 2.9 cm/s in the study group and to 11.1 ± 6.1 cm/s in the control group. In the prostatic fluid and ejaculate in both groups, the number of lecithin grains was increased after treatment. Examination and palpation of the scrotum showed no signs of hypogonadism and varicose veins of the spermatic cord, but some pastosity of the testicles and epididymides, which were apparently associated with a pre-

Table 2

Changes in sex and gonadotropic hormones over time in men in the test and control groups ($M \pm m$)

Таблица 2

Динамика половых и гонадотропных гормонов у больных основной и контрольной групп ($M \pm m$)

Criterion and reference value	Study group ($n = 38$)		Control group ($n = 20$)	
	Before treatment	After 12 weeks	Before treatment	After 12 weeks
FSH, mMe/mL (1.37–13.58)	12.2 ± 5.6	8.3 ± 3.7	11.8 ± 6.7	10.1 ± 4.9
LH, mMe/mL (1.4–8.75)	4.9 ± 2.6	3.8 ± 2.1	5.2 ± 3.1	4.9 ± 3.0
Total testosterone, nmol/L (>12)	11.9 ± 5.8	13.4 ± 5.6	12.8 ± 7.4	12.9 ± 6.2

Table 3

Changes in results of Doppler ultrasound of the prostate and testicles over time in patients in the main and control groups ($M \pm m$)

Таблица 3

Динамика результатов ультразвуковой доплерографии предстательной железы и яичек у больных контрольной и основной групп ($M \pm m$)

Doppler ultrasonography parameter	Study group ($n = 38$)				Control group ($n = 22$)				Reference values	
	Prostate gland		Testicles		Prostate gland		Testicles		Prostate gland	Testicles
	Before treatment	After 12 weeks	Before treatment	After 12 weeks	Before treatment	After 12 weeks	Before treatment	After 12 weeks		
V_{\max} , cm/s	6.9 ± 3.8	9.8 ± 2.9	6.2 ± 2.5	13.1 ± 3.2	6.9 ± 4.1	11.1 ± 6.1	8.2 ± 5.0	9.9 ± 5.1	4.5–12.5	8.5–14.5
Resistance index	0.712 ± 0.386	0.610 ± 0.383	0.852 ± 0.364	0.650 ± 0.342	0.701 ± 0.403	0.690 ± 0.398	0.702 ± 0.512	0.600 ± 0.497	0.64–0.68	0.50–0.66
Pulsatility index	1.290 ± 0.712	1.112 ± 0.686	2.137 ± 1.633	1.102 ± 0.746	1.212 ± 0.988	1.056 ± 0.922	1.520 ± 1.122	1.124 ± 0.967	1.12	2.1

vious epididymitis caused by STIs, was noted. On ultrasonography, the testicles and epididymides were of normal size of 43–44 mm with regular borders and a fine-grained structure. Doppler ultrasonography of testicular arteries before treatment showed some decreases in V_{\max} , which was more prominent in the study group than in the control group (6.2 ± 2.5 cm/s and 8.2 ± 5.0 cm/s, respectively), and an increase in the resistance index (0.852 ± 0.364 and 0.702 ± 0.512 , respectively). These findings are probably associated with previous diseases of accessory sex glands caused by STIs. After 12 weeks, the blood flow rate in testicular arteries increased to 13.1 ± 3.2 cm/s in the study group and to 9.9 ± 5.1 cm/s in the control

group, and resistance index values decreased in both groups (Table 3).

Tolerability of treatment was satisfactory in both groups; none of the patients had any adverse reactions associated with the drugs.

DISCUSSION

The therapeutic effect of multicomponent complexes AndroDoz and Testogenon was demonstrated in the reduction of DNA fragmentation and the number of morphologically altered forms of sperm cells, increase of their concentration and motility, improvement of blood circulation in the prostate gland and testicles, and a significant increase in the reproduc-

tive performance of the married couple. An increase in the total testosterone level and an improvement in the quality of erections were noted during the treatment course. The reason for the improvement in sexual function is apparently the increase in NOS activity in the smooth muscles of the cavernous bodies of the penis. Carnitine; zinc; vitamins A, E, and B₅; extracts of Pygeum bark; and flavonoids, which are components of AndroDoz and Testogenon, increased reproductive, hormonal, and copulatory functions as confirmed by subjective and objective criteria. The synergism of the action of the AndroDoz and Testogenon components has a positive effect on the hypothalamus–pituitary–gonadal system. They normalize the hormonal and functional states of the testicles, epididymides, and prostate gland and stimulate their own testosterone production by Leydig cells. After a 12 week course of combination therapy with AndroDoz and Testogenon, there was a decrease in oxidative stress parameters and a decrease in the risk of damage to the structure of the sperm cell and cell wall DNA of the epithelial cells of the prostate gland.

CONCLUSION

Thus, the results of the study showed high efficacy and good tolerability of combined therapy with AndroDoz and Testogenon in patients with impaired fertility and moderate androgen deficiency with a history of STI. We suppose that a course of treatment with these drugs twice a year in patients with STI-associated reproductive and sexual disorders is reasonable.

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