

**DIAGNOSTICS OF THE ACTIVITY OF THE ACCESSORY GLANDS OF THE MALE
GENITAL SYSTEM IN INFERTILITY**

Yarmukhamedov A. S., Faizullaeva N. Ya. and Musakhodzhaeva D. A.*

Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan, Tashkent, Uzbekistan.

*Corresponding Author: Musakhodzhaeva D. A.

Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan, Tashkent, Uzbekistan.

Article Received on 23/09/2020

Article Revised on 13/10/2020

Article Accepted on 02/11/2020

ABSTRACT

Background: In the structure of infertile marriage, the tendency towards an increase in the male factor and a deterioration in sperm quality dictates the need for a close study of the existing problem. **Objective:** We examined 72 patients with impaired fertility, who were aged from 26 to 45 years with diagnoses of oligo-, astheno-, teratozoospermia. **Methods:** Diagnosis verification was carried out on the basis of clinical, instrumental and laboratory research methods. A biochemical analysis of semen was carried out - the level of citric acid, fructose and zinc was studied to assess the functional capabilities of the prostate gland. **Result:** A significant decrease in the level of citric acid, fructose and zinc in the semen was revealed, as well as a decrease in the level of inhibin B in the blood serum. **Conclusion:** Summarizing the data presented, we can assume a probable mechanism for the development of shifts associated with impaired fertility, in which there is a decrease in the level of fructose, citric acid and zinc. At the same time, a decrease in the level of inhibin B in the blood serum is observed. All these changes lead to the activation of phospholipase A2, the production of which is indirectly related to the content of zinc ions; this process is due to the activation of free radical processes in the organs of spermatogenesis and ejaculate. Careful monitoring of spermatozoa, the study of their changes at the structural level, as well as the study of biochemical parameters that can discriminate pathological changes are the priority tasks of laboratory diagnostics.

KEYWORDS: semen, fructose, citric acid, zinc, serum inhibin B, sperm motility.**INTRODUCTION**

In the structure of infertile marriage, the tendency towards an increase in the male factor and a deterioration in sperm quality dictates the need for a close study of the existing problem. Infertility is a polietiological disease and requires modern universal markers, the study of the level of which would make it possible to determine the appropriate tactics for managing patients with impaired fertility, assess the prognosis and the prospects of treatment.^[1,3,4,10,23] A biochemical study of ejaculate makes it possible to assess the activity of the accessory glands of the male reproductive system and the hormonal status of the body as a whole, which is important in assessing the pathology of spermatogenesis. Zinc is found in large quantities in semen and prostate secretions and is of particular importance for the normal anatomical and functional state of the male reproductive system. This microelement is involved in the formation of sensitivity to various hormones and growth factors, is involved in the regulation of the activity of sperm plasma enzymes.^[2,5,6,22,25] Zinc promotes the processes of coagulation and liquefaction of ejaculate, inhibits spontaneous agglutination of sperm; increases sperm

motility, is important in ensuring the antibacterial activity of semen. The concentration of zinc in the secretion of the prostate gland depends on the level of androgens. From the prostate gland, zinc enters the seminal fluid, where its content is considered an accurate indicator of the organ's secretory activity. The body of an adult contains about 2-3 g of zinc and almost 40% of its total amount - in the prostate gland and ejaculate. It is the content of zinc in semen that is the limiting factor in male infertility. Zinc deficiency causes inhibition of production and, accordingly, the release of hormones - LH and FSH, which are directly involved in the regulation of testosterone levels.^[7,21,24]

Inhibin B is a known endocrine marker for assessing spermatogenesis. Sensitivity and specificity are important parameters for clinical decision making and avoiding traumatic biopsies. Evaluation of inhibin B levels should become an alternative to testicular biopsy, and can also be used in the differential diagnosis of male infertility.^[4,17,22]

The role of the biochemical study of semen is clearly underestimated, but often it is the study of semen that can reveal the causes of reproductive dysfunction in men, and therefore provide early diagnosis, determination of therapy tactics, and possibly outline new ways of treatment.^[7-9] This issue has been studied fragmentarily^[10-13], in connection with which further research and the search for other causes of pathospermia are relevant.

The aim of the work was to assess the parameters of biochemical markers of seminal plasma (citric acid, fructose and zinc) and inhibin B hormone in blood plasma of infertile men.

MATERIALS AND RESEARCH METHODS. The results of examination of 72 men with impaired fertility were analyzed. All patients were between 26 and 45 years old with diagnoses of oligo-, astheno-, teratozoospermia. Verification of the diagnosis was carried out on the basis of complaints, collection of anamnesis and examination, clinical and instrumental research methods, general blood and urine tests, biochemical parameters of seminal fluid, determination of the level of hormones in blood serum, examination for the presence of a bacterial-viral infection, as well as ultrasound of the scrotum organs, kidney and doppler sonography of the veins of the spermatic cord (to exclude varicocele). The control group consisted of 20 apparently healthy men with normal sperm counts. Mathematical processing of the data was carried out by the methods of variation statistics using standard mathematical software packages on a personal computer with the determination of the mean, its error, and Student's T criterion.

RESULTS AND ITS DISCUSSION. Taking anamnesis showed that none of the patients was exposed to ionizing radiation and did not use drugs, and there was no systematic use of alcohol.

The men with infertility we examined had a number of concomitant diseases. Diseases of the gastrointestinal

tract were observed in 28.0% (21/75) of patients, allergic diseases - in 20.0% (15/75), diseases of the cardiovascular system - in 10.7% (8/75), diseases bronchopulmonary system (upper and lower respiratory tract) - in 38.7% (29/75), diabetes mellitus - in 2.7% (2/75).

Laboratory studies of the hormonal levels in the examined men of the main group revealed an imbalance in the synthesis of female and male sex hormones in 37.3% (28/75).

Analysis of urological diseases revealed a number of pathologies associated with reproductive function.

Various forms of thyroid disease were observed in 28.5% of men. 18.3% of men complained of diseases of the gastrointestinal tract. Chronic pyelonephritis was noted in 24.2% of men. Cardiovascular diseases were recorded in 20.0% of men. 9.7% of men suffered from Chronic rheumatism. 22.6% of men complained on various allergic diseases.

On examination, the patients didn't show any external signs of hypogonadism. On palpation of the scrotal organs, a normal testicular volume was noted.

Ultrasound of the prostate gland showed ultrasound signs of chronic prostatitis in 62.7% of patients. The results of ultrasound of the scrotum organs showed no pathological changes.

The results of spermogram examination are shown in Fig. 1. As can be seen from the above data, before treatment the concentration of spermatozoa was 13.7 million / ml, in 3.2 ml of ejaculate, which was significantly lower than the control values ($P < 0.05$). sperm analysis of the morphologically normal forms according to Kruger showed that in patients it is 2.7%, significantly lower than the control values ($P < 0.05$).

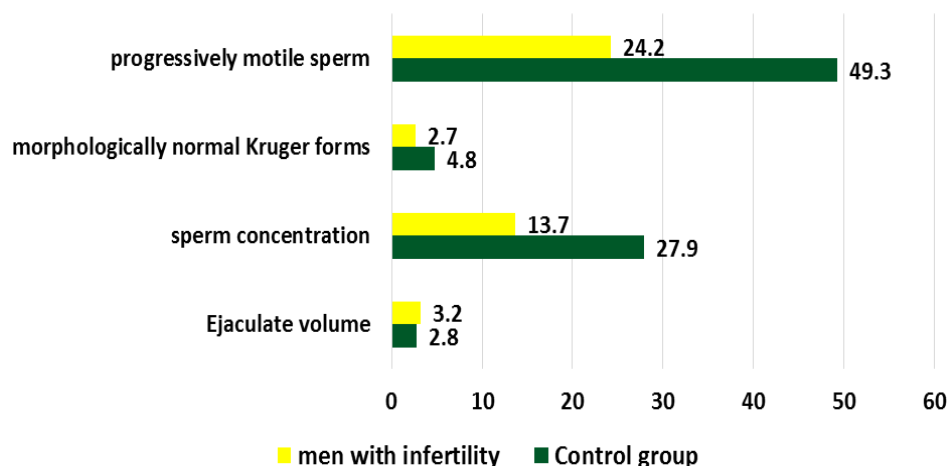


Fig 1: Ejaculate indicators in the surveyed men.

The number of motile spermatozoa was 2 times less in patients than in the control group ($P < 0.01$).

In 47 (62.7%) patients, an increase in ejaculate viscosity was noted, which was caused either by a decrease in the volume of the ejaculate, or by a high content of mucus in it. According to researchers^[3, 4], the viscosity of the ejaculate in oligoasthenoospermia was significantly higher than in normozoospermia. An increase in the viscosity of ejaculate in humans reduces the fertilizing ability of sperm.^[2, 4] This is explained, on the one hand, by the fact that the increased viscosity of the ejaculate can interfere with the movement of spermatozoa in the mucus^[2], and on the other hand, it can be combined to varying degrees with other types of violations of the fertilizing ability of sperm.^[3,4]

In 9 (12.0%) patients, a decrease in ejaculate viscosity was noted, which is associated with impaired enzymatic, generative and endocrine functions of the testicles.^[1]

When calculating the number of leukocytes in the ejaculate of patients, their level was significantly increased than in healthy people ($P < 0.01$).

All men with infertility (table 1) showed a decrease in the concentration of fructose in the ejaculate (7.4 ± 0.5 mmol/L) compared with the norm (15.0 ± 0.9 mmol/L, $P < 0.01$).

Table 1: Biochemical parameters of spermogram in infertility.

Parameters, mmol/l	Men with infertility (n = 75)	Control group (n = 20)
Fructose	7.4 ± 0.5	15.0 ± 0.9 *
Citric acid	18.3 ± 1.3	23.4 ± 1.8 *
Zinc	1.9 ± 0.3	3.7 ± 0.8 *

Note: * - reliability of data in relation to the control group ($P < 0.01$)

There was also a decrease (18.34 ± 1.27 mmol / ml) in the concentration of citric acid in the ejaculate compared to the norm (23.42 ± 1.83 mmol / ml, $p < 0.05$).

A decrease in the concentration of fructose and citric acid in the ejaculate indirectly indicates the presence of degenerative changes in the accessory gonads and hypoandrogenism in men with infertility.

The participation of zinc ions in neuroendocrine regulation proves that under conditions of zinc deficiency, inhibition of production and, accordingly, the release of luteinizing and follicle-stimulating hormones, which are directly involved in the regulation of testosterone levels, affects Leydig interstitial cells, which regulate and stimulate spermatogenesis in the convoluted tubules. [Olina A.A., 2015].

A decrease in the content of zinc in semen leads to changes in intracellular metabolism, manifested in a decrease of the kinetic capabilities of spermatozoa in the ejaculate of patients, which is a natural pathophysiological process. According to the data obtained, an almost 2-fold decrease in zinc ions was found in infertile men (1.9 ± 0.3 versus 3.7 ± 0.8 mmol / l; $P < 0.01$).

A decrease in the content of zinc in semen leads to changes in intracellular metabolism, manifested in a decrease of the kinetic capabilities of spermatozoa in the ejaculate during infertility. Summarizing the data presented earlier, we can assume a probable mechanism for the development of the observed shifts associated with the fact that when fertility is impaired, phospholipase A2 is activated, the production of which is indirectly related to the content of zinc ions; this process is due to the activation of free radical processes in the organs of spermatogenesis and ejaculate, as indicated by the results of previous studies [World Health Organization. 2001.].

The hormonal background of a man is one of the most important indicators for the normal functioning of his body. In the process of its formation, a large number of different hormones are produced, which determine not only the physical, but also the sexual health of a man, among them inhibin is of a certain importance [Grunevald S., 2013; Barbotin A. L., 2015].

Inhibin is a non-steroidal hormonal protein produced in the body of any person. In males, inhibin production occurs in the Sertoli cells located in the seminal ducts. It was found that with overactive spermatogenesis inhibin oppresses the FSH produced by the pituitary gland and, conversely, with low spermatogenesis, the level of the hormone in the blood increases significantly. At one time FSH is a stimulant of inhibin production, which determines a close relationship between them [Kadyrov, 2016; Likhonosov N.P., 2019; McNeilly A., 2012; Huang X., 2012].

When studying the level of inhibin B in the blood serum, a significant decrease was found in infertile men ($p < 0.001$), the data obtained are presented in diagram 2.

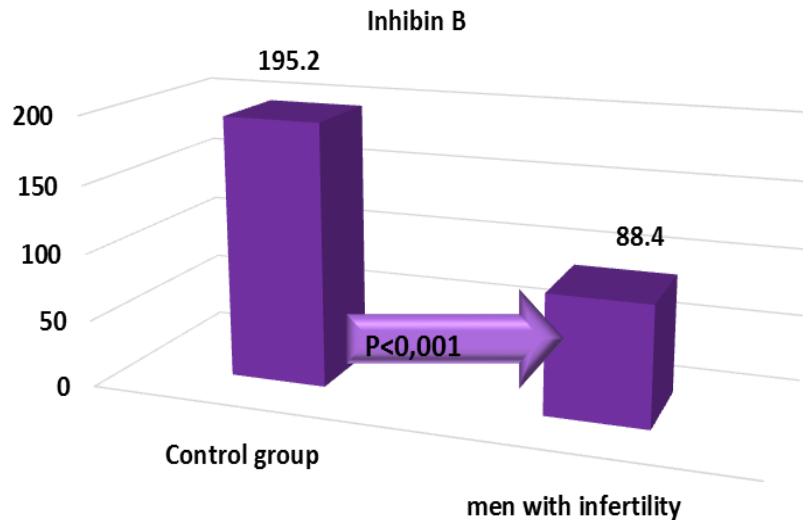


Figure 2: The content of inhibin B in blood serum with infertility in men, n/g.

Summarizing the data presented, we can assume a probable mechanism for the development of shifts associated with impaired fertility, in which there is a decrease in the level of fructose, citric acid and zinc. At the same time, a decrease in the level of inhibin B in the blood serum is observed. All these changes lead to the activation of phospholipase A2, the production of which is indirectly related to the content of zinc ions; this process is due to the activation of free radical processes in the organs of spermatogenesis and ejaculate. Careful monitoring of spermatozoa, the study of their changes at the structural level, as well as the study of biochemical parameters that can discriminate pathological changes are the priority tasks of laboratory diagnostics.

Thus, studies of the concentration of inhibin B in blood plasma, citric acid, fructose and zinc in seminal plasma can be used in a comprehensive examination of patients to clarify the therapeutic and diagnostic tactics, which will identify the causes of abnormal reproduction of androgens, disturbances in the morphology of spermatozoa, pathologies of glandular organs. and outgoing channels.

BIBLIOGRAPHY

1. Aizikovitch B.I., Ustinov D.V., Antonov A.R. The relationship of the cytokine and micro element profile with the quality of seminal plasma. *Novosibirsk State University Bulletin. Series: Biology, Clinical Medicine*, 2010; 8(4): 76-82.
2. Borisov V.V. Male infertility. The use of zinc and antioxidants in the treatment of fertility disorders and inflammatory diseases of the male genitalia (clinical lecture). *Consilium Medicum*, 2015; 17(7): 16-23.
3. Vityazeva I.I. Treatment of infertility in men with non-obstructive azoospermia by the method of microdissection technique of sperm extraction from testicular tissue in the in vitro fertilization program using the technique of intraplasmic injection of a single sperm. *Literature review. Andrology and Genital Surgery*, 2014; 2: 6-22.
4. Galimova E.F., Akhmadullina G. Kh., Bulygin K.V., Mochalov K.S., Galimov Sh. N. Inhibin B and activin A in the pathogenesis of idiopathic infertility in men. *Kazan Medical Journal*, 2015; 5 (96): 749-52.
5. Gizinger O.A., Letyaeva O.I., Nikushkina K.V., Frantseva O.V., Zabiroya M.R. Decreased sperm activity as a result of infectious and inflammatory diseases of the urogenital tract of men. *Laboratory diagnostic methods. Correction of the inflammatory process and kinetic functions of spermatozoa using low-intensity laser therapy. Bulletin of the Chelyabinsk Regional Clinical Hospital*, 2013; (2): 58-60.
6. Glybochko P.V., Alyaev Yu. G., Chaly M.E., Akhvlediani N.D. *Sexual disorders in men. - M.: GEOTAR-Media 2012. - pp. 71–90.*
7. Gorpinchenko I.I., Gurzhenko Yu.N., Spiridonenko V.V. Optimization of indicators of the secretion of the prostate gland and ejaculate in male infertility against the background of chronic prostate vesiculites // *Men's health*, 2014; 3(50): 68-74.
8. Kadyrov Z.A., Moskvichev D.D., Faniev M.V. Inhibin B indices in blood serum in infertile patients // *Andrology and genital surgery*, 2016; T. 17(1): C. 23-27.
9. Kasatonova E.V., Efremov E.A., Melnik Y. I., Zaletova V.V., Mskha-laya G. Zh. Experience of microsurgical biopsy of the testicle and its epididymis in patients with non-obstructive azoospermia. *Experimental and Clinical Urology*, 2014; 4: 38-41.
10. Korneev I.A., Zasseev R.D., Shevchuk I.G., Pelipeychenko A.A. Prevalence of sexually transmitted infections in men in infertile marriages // *Urological Bulletin*, 2018; T. 8(2): S. 30-35.

11. Lipatova N.A., Rakov S.S., Morozova V.T. Protein markers of sperm plasma in laboratory diagnosis of infertility in diseases of the male reproductive system // *Clinical laboratory assistant. Diagnostics*, 1998; 2: C. 15-16.
12. Likhonosov N.P., Ayub A.Kh., Babenko A.Yu., Borovets S.Yu. The role of Inhibin B in the regulation of spermatogenesis and its clinical significance in male infertility // *Urological Bulletin*, 2019; T.9(1): S. 39-44.
13. Neimark S.A., Aliev R.T. Significance of the study of enzymes-sperm plasma in the pathogenesis of relative male infertility // *Urology*, 2000; 3: P. 34–37.
14. Olina A.A., Sadykova G.K. The importance of zinc deficiency in the formation of reproductive health disorders (literature review). *Perm Medical Journal*, 2015; 32(5): 138-43.
15. Trifonova Yu.P., Boyko M.I. Vilno-radical processes in sperm children with chronic prostatitis dota pislyalikuvannya // *Bulletin of Sumskohoder. univer.;* "The medicine", 2005; 3(75): - S. 167-169.
16. Trifonova Yu.P., Boyko M.I. Evaluation of radical processes in sperm cholovites from secretory "toxic and non-promiscuous diseases" // *Zbirn. Sciences*, 2003;– C. 9–11.
17. Barbotin A. L., Ballot C., Sigala J., Ramdane N., Duhamel A., Marcelli F., et al. The serum inhibin B concentration and reference ranges in normozoospermia. *Eur J Endocrinol*, 2015; 172(6): 669-76. DOI: 10.1530/EJE-14-0932.
18. Björndahl L., Kvist U. Structure of chromatin in spermatozoa // *Adv. Exp. Med. Biol*, 2014; 791: P. 1–11.
19. Cavallini G. Male idiopathic oligoasthenoteratozoospermia // *Asian. J Androl*, 2006; № 8(2): P. 143–57.
20. Grunewald S., Glander H-J., Paasch U., Kratzsch J. Age-dependent inhibin B concentration in relation to FSH and semen sample qualities: a study in 2448 men. *Reproduction*, 2013; 145(3): 237-44.
21. Henkel R., Maass G., Schuppe H.C. et al. Seasonal changes of neutral alpha-glucosidase activity in human semen // *J. Androl*, 2006; № 1: P. 34–39.
22. Huang X., Bai Q., Yan L., Zhang Q., Geng L., Qiao Dr. J. Combination of serum inhibin B and follicle-stimulating hormone levels can not improve the diagnostic accuracy on testicular sperm extraction outcomes in Chinese non-obstructive azoospermic men. *Chin Med J (Engl)*, 2012 Aug 125(16): 2885-9.
23. McNeilly A. Diagnostic applications for inhibin and activins. *Mol Cell Endocrinol*, 2012; 359: 121-5. DOI: 10.1016/j.mce.2011.06.017.
24. Mitchell V., Robin G., Boitrelle F., Massart P., Marchetti C., Marcelli F., et al. Correlation between testicular sperm extraction outcomes and clinical, endocrine and testicular histology parameters in 120 azoospermic men with normal serum FSH levels. *Int J Androl*, 2011 Aug; 34(4): 299-305.
25. World Health Organization. Manual for the standartized investigation and diagnosis of the infertile couple. Cambridge: Cambridge University Press, 2001.