CHANGES IN THE SPERMOGRAM IN MEN WITH INFERTILITY AND VARICOCELE WITH ASYMPTOMIC INFECTIONS OF THE GENTRICAL SYSTEM

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ИЗМЕНЕНИЕ СПЕРМОГРАММЫ У МУЖЧИН С БЕСПЛОДИЕМ И ВАРИКОЦЕЛЕ ПРИ БЕССИМПТОМНЫХ ИНФЕКЦИЯХ МОЧЕПОЛОВОЙ СИСТЕМЫ

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Annotation. Infertility is a hot topic in medicine, affecting 12 to 20% of couples in the world. In approximately 50% of cases, the cause of infertility is male factor [1, 4]. Despite numerous studies, the etiology of male infertility often remains unknown. According to available data, up to 30% of all cases of male infertility are associated with varicocele [2, 7]. The role of concomitant infections of the urogenital tract (UTI) in infertility in combination with varicocele has not been sufficiently studied.

Key words: spermogram, infertility, varicocele, genitourinary system infections.

Аннотация. Бесплодие является актуальной темой медицины, которая затрагивает от 12 до 20 % семейных пар в мире. Приблизительно в 50 % случаев

причиной бесплодия является мужской фактор [1, 4]. Несмотря на многочисленные исследования, этиология мужского бесплодия часто остается неизвестной. Согласно имеющимся данным с варикоцеле ассоциированы до 30 % всех случаев мужского бесплодия [2, 7]. Роль сопутствующих инфекций урогенитального тракта (УГТ) при бесплодии в сочетании с варикоцеле недостаточно изучена.

Ключевые слова: спермограмма, бесплодлие, варикоцеле, инфекции мочеполовой системы.

Introduction. Currently, several different methods are used to treat varicocele, but success is not always achieved. One of the possible reasons for unsuccessful treatment of infertility combined with varicocele may be concomitant infections of the urogenital tract (UGT) [1, 5, 16]. This assumption is based on results showing that the presence of bacteria and viruses in the UGT of men in the absence of clinically pronounced signs of an infectious disease negatively affects sperm parameters and fertility.

Purpose of the work: to assess the impact of bacterial and viral infections of the UGT on ejaculate parameters in patients with varicocele and infertility.

Materials and methods. The study included 75 patients who applied for examination. As a result of clinical and laboratory analysis, primary infertility and varicocele were discovered in 49 patients (mean age 30.2 ± 4.9 years). The comparison group consisted of 26 practically healthy men (average age 31.5 ± 8.6 years). All patients had no clinical manifestations of infectious diseases.

In men with varicocele, infertility was diagnosed if, after 12 months of regular sexual activity without contraception, the partner did not become pregnant.

Ejaculate samples from 75 examined men were obtained by masturbation after 3 days of sexual abstinence and divided into 2 parts: the 1st was used for spermiological analysis, the 2nd was used for DNA extraction from whole ejaculates with subsequent detection of viral DNA. In addition, the most common bacterial pathogens were determined in urogenital materials (scrapings from the urethra).

The main spermogram indicators (concentration and degree of sperm motility, the number of morphologically normal forms of sperm) were studied in 38 patients with infertility and varicocele and in 26 practically healthy men.

The DNA of human papillomaviruses of high carcinogenic risk in clinical material was determined by PCR.

A real-time PCR reagent kit was used to quantify Epstein-Barr virus, cytomegalovirus (CMV) and human herpes virus 6 (HHV-6) DNA. The p-globin gene was used as an endogenous internal control.

Results. Markers of infectious agents were not found in ejaculate samples obtained from apparently healthy men. Data on the frequency of occurrence of pathogens of the studied bacterial and viral infections in 49 patients with infertility and varicocele showed that in the majority (55.1%) of patients, bacteria and viruses were not found in urogenital materials Bacterial markers were detected in 15 (30.6%) patients. DNA of HPV HRV or human herpes viruses was detected in the ejaculate of 7 (14.3%) of 49 patients examined.

The most common bacterial and viral pathogens have been identified.

Among bacteria, causative agents of chlamydial infection were more often identified ($p < 0.05$). The causative agents of viral infections were relatively rare and with approximately the same frequency.

Quantitative DNA analysis of 3 human herpes viruses revealed significant variability in their concentrations in ejaculates: the minimum value was 450 copies (2.65 ^10/ml), the maximum was 11,750 copies (4.07 ^10/ml). The median for all positive samples was relatively high - 5355 copies (3.73 ^10 / ml), while the concentration of CMV and HHV-6 DNA was higher than the concentration of EBV DNA. Among herpes viruses, CMV was found in higher concentrations than HHV-6 and EBV. Among herpes viruses, CMV was found in higher concentrations than HHV-6 and EBV. The results of quantitative analysis of HPV HCR DNA showed that the median values were low and did not reach the clinically significant viral load, which was taken as 3 ^10 / ml.

For the purpose of spermiological study and based on the data obtained, patients with infertility and varicocele were divided into 3 groups: 1st group consisted of 18 men without clinical and laboratory signs of inflammatory diseases of UGT, 2nd group - 14 patients in whom urethral scrapings were found representatives of the bacterial flora, but there were no clinical signs of infectious diseases, 3rd - 6 patients without clinical signs of inflammatory diseases of UHT, but in whose semen viral DNA was detected. Group 4 (comparison) included 26 practically healthy men.

Statistical analysis showed that the average values of concentration, motility and number of morphologically normal forms of sperm in the ejaculates of men of the 4th group were significantly higher than in other groups (for each spermogram indicator $p < 0.05$). The quality indicators of ejaculate from patients in groups 1 and 2 were not statistically significantly different ($ > 0.05). At the same time, the number of morphologically normal forms of sperm in group 2 was lower compared to group 1 (<0.05). The greatest changes were found when comparing the main spermogram parameters in patients of the 3rd group. Thus, the concentration of sperm was 1.8 times lower than in groups 1 and 2, and the number of morphologically normal cells was 2.2 times less than in group 1; the differences are statistically significant ($p < 0.05$).

The data obtained showed that in patients of the 1st group in most cases (33.3%) normozoospermia was established, while in patients of the 2nd group - asthenoteratozoospermia. With viral infection of the ejaculate, such forms of pathology as teratozoospermia, asthenoteratozoospermia and oligoteratozoospermia occurred with equal frequency.

Due to the large proportion of patients who showed a decrease in the number of morphologically normal sperm, more detailed microscopic analysis was performed. We identified 14 abnormalities in the structure of spermatozoa, including: atypia of the flagellum, amorphous heads, elongated heads, microheads, cytoplasmic drop on the head, heteroaxiality, round heads, drop on the neck, abnormalities in the acrosome and two-headed sperm. Combined disorders were also found: amorphous heads with atypia of the flagellum, a drop on the neck with atypia of the flagellum, a drop on the neck with disturbances in the acrosome; disturbances in the acrosome with atypia of the flagellum.

For each patient, the average number of abnormalities in the structure of spermatozoa was calculated, as well as the number of cells with non-standard morphology. It turned out that the greatest disturbances occurred in the structure of the sperm head compared to the neck and flagellum. At the same time, the average number of cells with abnormalities in the morphology of the sperm head in patients of groups 2 and 3 was significantly higher (77.8 and 66.7%, respectively) than in men of group 1 (29.8%); the differences are statistically significant ($p < 0.05$).

Discussion. The incidence of varicocele in the general population is 10-20%. Among men with varicocele, 35-40% suffer from primary and up to 80% secondary infertility [3, 14, 15]. Important criteria in the diagnosis of male infertility are spermogram indicators such as sperm concentration, their overall motility and the number of morphologically normal forms. Published data indicate a negative effect of varicocele on sperm quality [2, 6, 10].

According to epidemiological studies, more and more men with infertility suffer from inflammatory diseases of the UGT, which are often asymptomatic [1, 8, 13]. It was noted that in patients with infertility and varicocele, in whose UGT bacteria and viruses were detected, sperm counts were statistically significantly reduced compared to patients with a similar diagnosis, but without infectious agents. A comparative analysis of the main indicators of spermograms with varicocele without infections and with a bacterial genital infection without varicocele showed that both conditions worsen sperm quality [1, 9, 11]. It has been established that the presence of bacteria in sperm during asymptomatic infection has a negative effect on fertilization both through a direct effect on gametes and indirectly through immune mechanisms.

Our analysis of morphological abnormalities in the structure of sperm allows us to judge the cellular and molecular mechanisms of decreased fertility in varicocele

associated with UGT infections. Thus, a violation of the stages of meiosis indicates a block of spermatogenesis. The detection of intracellular vacuoles, an atypical head structure and a defective acrosome, as well as hyperconcentration of chromatin in the examined patients indicate a decrease in the ability of sperm to fertilize and further normal development of the zygote. Disturbances in the formation of the neck, including a cytoplasmic drop on the neck, indicate immature forms in the ejaculate, and an atypical structure of the flagellum indicates a decrease in sperm motility.

Conclusions. In case of male infertility associated with varicocele, laboratory diagnosis of bacterial and viral pathogens that are most often found in UGT of men can be recommended, even in the absence of clinical signs of infection. A quantitative analysis of pathogens in the UGT, carried out before treatment of varicocele, will determine the need for etiotropic therapy for a latent infection. Further research is required to assess the effect of infectious pathology on the effectiveness of infertility treatment for varicocele.

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