DOI 10.26724/2079-8334-2021-2-76-203-206
UDC 616.681:591.463.4

B.V. Grytsuliak, V.B. Grytsuliak, N.V. Bielova, O.Ya. Hlodan, N.P. Dolynko, I.Yo. Ivasiuk
Vasyl Stefanyk Precarpathian National University, Ivano-Frankivsk

CHANGES IN SPERMATOGENESIS IN INFERTILE MIDDLE AGE MEN WITH BENIGN PROSTATIC HYPERPLASIA

e-mail: vita.ivasiv11@gmail.com

It is established that in men aged 40-50 years already occur signs of benign prostatic hyperplasia with an increase in its volume to (51.2±2.0) and weight – up to (48.3±1.6) g. Cytohistological changes in it are manifested by an increase in the area of stromal components with a decrease in the area of the glandular component up to 56.5 % and 43.5 %, respectively. Under these conditions, arterial blood flow velocity is reduced more than twice (7.70 cm/s vs. 16.5 cm/s) and volumetric blood flow is reduced to 0.03 l/min versus 0.06 l/min. Under these conditions, the testicles are likely to have reduced hemodynamic parameters, reduced testicular volume, diameter of convoluted seminiferous tubules, the number of living, morphologically normal and actively motile spermatozoa and testosterone concentrations in the blood.

Key words: testicles, hemodynamics, spermatogenesis, benign prostatic hyperplasia.

Б.В. Грицуляк, В.Б. Грицуляк, Н.В. Бєлова, О.Я. Глодан, Н.П. Долинко, І.Й. Івасюк

ЗМІНИ СПЕРМАТОГЕНЕЗУ В НЕПЛІДНИХ ЧОЛОВІКІВ ЗРІЛОГО ВІКУ ПРИ ДОБРОЯКІСНІЙ ГІПЕРПЛАЗІЇ ПЕРЕДМІХУРОВОЇ ЗАЛОЗИ

Встановлено, що вже у чоловіків віком 40-50 років наявні ознаки доброякісної гіперплазії передміхурової залози зі збільшенням її об'єму до (51,2±2,0) і маси – до (48,3±1,6) г. Цитогістологічні зміни у ній проявляються збільшенням площі стромальних компонентів зі зменшенням площі залозистого компонента до 56,5 % та 43,5 % відповідно. За цих умов більше як у два рази (7,70 см/с проти 16,5 см/с) знижуються показники швидкості артеріального кровотоку та до 0,03 л/хв проти 0,06 л/хв – об'ємного кровотоку. За цих умов, в яєчках вірогідно знижуються показники гемодинаміки, зменшується об'єм яєчок, діаметр звивистих сім'яних трубочок, кількість живих, морфологічно нормальних і активно рухливих сперматозоїдів та концентрація тестостерону у крові.

Ключові слова: яєчка, гемодинаміка, сперматогенез, доброякісна гіперплазія передміхурової залози.

The work is a fragment of the research project "Current aspects of andrology and correction of spermatogenesis", state registration No. 0119U103671.

It is known that prostate diseases are an important problem in urology and andrology. According to the literature, men in the first period of adulthood, 22–35 years, are more frequently diagnosed with acute and chronic prostatitis, which is associated with an increase in the incidence of various types of urethritis and epididymo-orchitis [1, 2]. In men of the second adulthood period f (36–60 years), chronic prostatitis is frequently combined with the development of benign prostatic hyperplasia. The latter, according to the literature [3, 4], is found in 50 % of men. The reasons for the development of benign prostatic hyperplasia have not been definitively established, but it is associated not only with chronic prostatitis, but also with hormonal imbalance, which is already manifested in men of the second adulthood period.

Under these conditions, the ratio between the stroma and parenchyma of the prostate changes [6] and disrupts the formation and release of biologically active substances into the blood, namely prostaglandins, which affect the production of sex hormones by the testes, spermatogenesis and increase sperm motility [9].

Despite the significant number of publications related to male infertility, our analysis shows that the features of hemodynamics, cytohistological changes in the testes and ejaculate in benign prostatic hyperplasia remain relevant.

The purpose of the study was to establish the nature of changes in hemodynamics in the prostate with benign hyperplasia and the impact on the adult men spermatogenesis.

Materials and methods. Ultrasound examination and color ultrasound angiography of the prostate and testicles in 12 infertile men aged 40–50 years, diagnosed with infertility and benign prostatic hyperplasia, were performed at the clinical diagnostic center "Prima MED" using the Siemens AWENSOL SIEMENS SON device, (Germany) with a sensor of 5–10 MHz. All morphometric parameters were recorded in sonograms. In the gray scale mode, the linear dimensions of the prostate and testicles were determined: length, width and thickness (mm), volume (cm^3) and weight (g).

In the mode of color Doppler mapping a quantitative assessment of the vessels diameter (VD) was performed. Qualitative indices of hemodynamics in them were: peak blood flow rate (PBFR) cm/s, diastolic blood flow rate (DBFR) cm/s, pulse index (PI) RU, resistance index (RI) RU, volumetric blood flow (VBF) l / min. Laboratory examination of ejaculate, histological and electron microscopic examination of prostate

and testicular biopsies of nine infertile men with benign prostatic hyperplasia, obtained in the urology department of the Ivano-Frankivsk Regional Clinical Hospital, in accordance with the agreement on cooperation, were performed using the standard methods.

According to the WHO technique (2010) modified by I.S. Chornokulsky, Yu.B. Tchaikovsky, MI Boyko, S.V. Basalitskaya (2013), ejaculate volume, sperm concentration, morphological characteristics, percentage of living forms, and their motility were determined. The testosterone concentration in the blood was examined by enzyme-linked immunosorbent assay using an IMMULITE-2000 automatic analyzer (Siemens Healthcare Diagnostics Inc., USA).

Statistical processing of morphometric parameters was performed using the Statistica 10 computer software. Comparison of the obtained values was performed using the Mann-Whitney U-test. The changes were considered significant at $p \leq 0.05$. The Commission on Biomedical Ethics of the Precarpathian National University did not find any violations of moral and ethical norms during the scientific work (Minutes No. 3 dated 16.10.2019).

Results of the study and their discussion. According to our observations, the echometric parameters of the prostate gland in men of this age group with manifestations of benign hyperplasia compared to the control group are likely to increase. In particular, its volume increases to (51.2±2.0) cm^3, and weight – to (48.3±1.6) g against (33.4±1.0) cm^3 and (39.0±1.5) g in men of this age in the control group.

According to color angiography, there is a significant (more than by 2 times) decrease in the peak rate of arterial blood flow – 7.70 cm/s against 16.5 cm/s in the control. Within the same limits, the diastolic blood flow rate is lower, which is 2.46 cm/s. Under these conditions, the volumetric blood flow decreases to 0.03 l/min against 0.06 l/min. in the control group [9].

In histological microslides of the prostate gland in this group of men, cytohistological changes are manifested by an increase in the area of stromal components with a decrease in the area of the glandular component to 56.5 % and 43.5 %, respectively (fig. 1). The size of the end sections of some tubular-alveolar glands decreases, and that of others on the contrary – expand with the certain areas emergence of both proliferation and atrophy of epithelial cells (fig. 1), which are manifestations of benign hyperplasia [9].

According to electron microscopy in the nuclei of secretory epitheliocytes, chromatin is non-condensed, the cytoplasm of cells has pronounced vacuolation, mitochondria are reduced (fig. 2).

According to color ultrasound angiography of the testicles in men with benign prostatic hyperplasia, the mean maximum blood flow rate in the testicular artery within the spermatic cord decreases to (15.6±1.0) cm/s, and in the testicular part of the artery – to (10.2±1.2) cm/s, against (18.5±1.5) cm/s and (12.0±1.0) cm / s, respectively, in the control group. Under these conditions, the mean minimum blood flow rate in the testicular artery is (6.2±0.4) cm/s and (5.0±0.2) cm/s, respectively.

Volume blood flow is reduced to (8.7±1.2) ml / s vs. (10.6±1.0) ml/s in the testicular artery. The mean linear blood flow rate in the testicular veins decreases to (7.0±0.5) cm/s, and the volumetric blood flow rate decreases to (8.0±0.8) ml/min [5, 7, 9]. The testis volume is reduced to (15.5±1.3) cm^3 versus (17.6±1.0) cm^3 in the control.

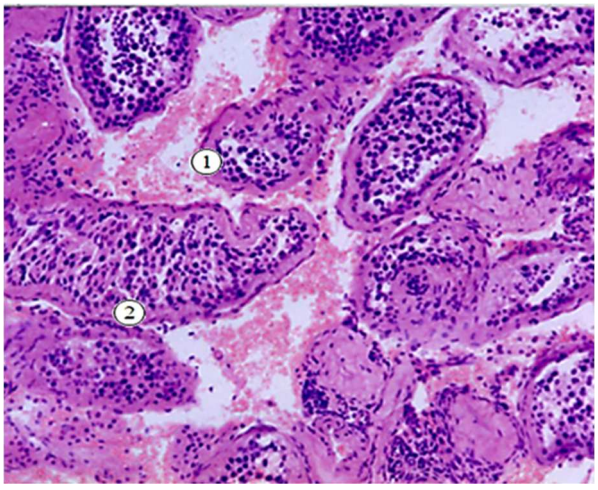

Fig.1. Thickening of its own membrane (1) and deformation of the convoluted seminiferous tubule (2) of the testis in a 50-year-old man with benign prostatic hyperplasia. Hematoxylin and eosin staining. Magn. x80.

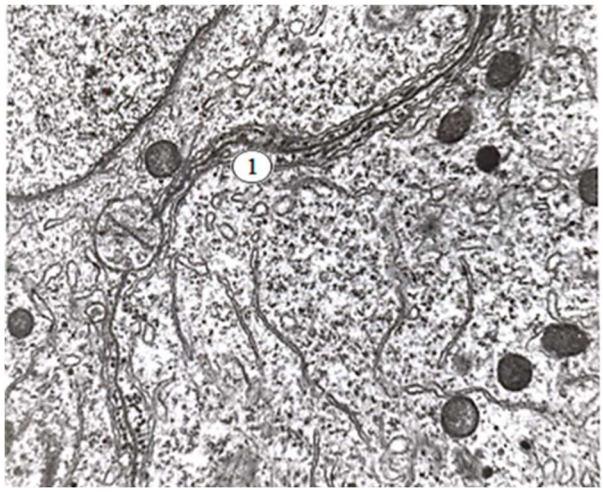

Fig.2. Approximation of the cytosolic membrane in the connective apparatus of the supporting epitheliocytes (1) in the testis of a 50-year-old man with benign prostatic hyperplasia. Magn. x12000.

In histological microslides obtained from testicular biopsies, the diameters of convoluted seminiferous tubule are (160.5±12.7) μm versus (196.9±10.3) μm in the control, and their own membranes

are significantly thickened. Supportive epitheliocytes and spermatogonia are found in more than half of these seminiferous tubules (fig. 3). There are small groups of interstitial endocrinocytes in the interductal connective tissue, which nuclei volume decreases to (72.5±3.6) μm^3 versus (90.2±1.5) μm^3 in the control. Plasma testosterone level is reduced to (370.0±9.0) ng/dL versus (590.0±30.0) ng/dL in the control.

According to electron microscopy of testicular biopsies, the own membrane in most of the convoluted seminiferous tubules is deformed. The basal membrane of the spermatogenic epithelium is thickened and hyalinized. Nuclei of myoid cells are of irregular shape, hyperchromic. Myofilaments are not detected in their cytoplasm.

Perinuclear condensation of chromatin in the nuclei of supporting epitheliocytes, spermatogonia and spermatids is preserved. The cytoplasm is vacuolated, in mitochondria the reduction of cristae, Golgi's sacs and tubules of the endoplasmic reticulum are narrowed. The structure of the supporting epitheliocytes' connecting apparatus is disturbed. Their cytolems are approximate, the cisterns of the endoplasmic reticulum are unevenly expanded, and the microfilaments are reduced (fig. 4).

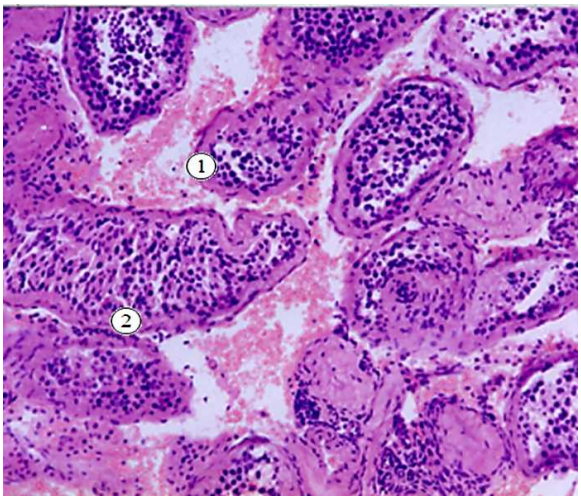

Fig.3. Thickening of their own membrane (1) and deformation of the convoluted seminiferous tubules (2) in the testis of a 50-year-old man with benign prostatic hyperplasia. Hematoxylin and eosin staining. Magn. x80

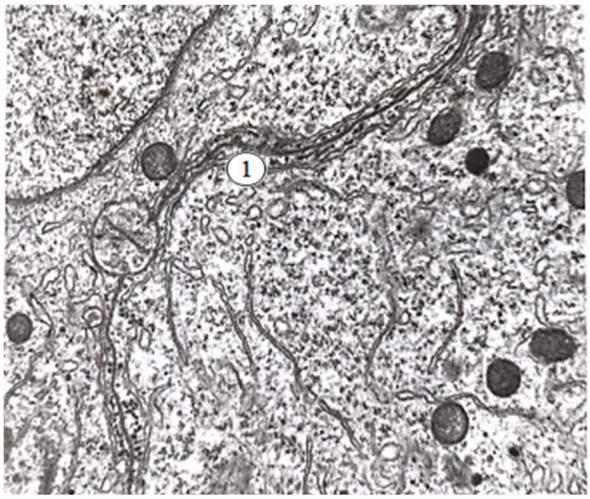

Fig. 4. Approximation of the cytosolic membranes in the connecting apparatus of the supporting epitheliocytes (1) in the testis of a 50-year-old man with benign prostatic hyperplasia. Magn. x12000.

The basal membrane of the testicular hemocapillaries is unevenly thickened, the cytoplasm of epitheliocytes is vacuolated, cristae are deformed in mitochondria, and elements of the Golgi complex and endoplasmic reticulum are expanded. Contours of the endotheliocytes' internal cytosolic membrane have deep protrusions into the lumen of the capillaries. Nuclei of endothelial cells of irregular shape with peripheral condensation of chromatin. The nuclei of interstitial endocrinocytes are hyperchromic, the cytoplasm is reduced, cytoplasmic organelles are deformed.

Studies of mature men ejaculate with signs of benign prostatic hyperplasia show that the volume of ejaculate is reduced to (2.0±0.5) ml, the concentration of spermatozoa – to (18.20±1.5) million/ml, the total number of spermatozoa – up to (64.06±5.4) million against (3.12±0.5) ml, (71.1±3.6) million/ml and (190.15±3.2)) million in the control. The number of morphologically normal spermatozoa decreases to 39.5 % vs. 71.2 %, the number of spermatozoa with head pathology increases to 27.3 % vs. 14.6 %, spermatozoa with pathology of the flagellum main part – up to 18.1 % vs. 13.5 %. Under these conditions, the proportion of living forms of sperm decreases to 56.1 % against 65.8 % in control, to 15.6 % – the number of spermatozoa with general progressive movement, against 27.5 % in the control and number of immobile spermatozoa increases to 45.8 % against 30.5 % ($p<0.05$) [7, 8].

Thus, our studies of the prostate in men of reproductive age are important for the clinic, as they occupy the third place in the structure of the genitourinary system's diseases. At this age, prostate adenoma has become widespread [1, 2], but its effect on spermatogenesis remains understudied.

In order to establish changes in the prostate and testicles, non-invasive methods were used – ultrasound and color angiography, which provide an opportunity to establish the parameters of the genitals and the nature of their hemodynamics changes. Having applied these clinical diagnostic methods, we confirmed that already in mature men there were signs of its benign hyperplasia – an increase in the organ's volume to (51.2±2.0) cm^3 and weight – to (48.7±1.6) g, comparing them to the parameters in the control group.

Under these conditions, color angiography of the prostate's blood vessels indicated a 2-fold decrease in the peak rate of arterial blood flow to 7.70 cm/s against 16.50 cm/s of peak arterial blood flow rate and up to 0.03 l/min. against 0.06 l/min – of volumetric blood flow. Disorder of hemodynamics in the

prostate gland caused a decrease in the area of the glandular component and an increase in the area of the stromal component [5, 6].

Given the importance of endocrine and exocrine prostate function in the regulation of spermatogenesis, we obtained important data for andrology concerning the nature of hemodynamic, cytohistological changes in the testes in benign prostatic hyperplasia in men of reproductive age and their effect on ejaculate parameters [3, 4].

We found that under these conditions, hemodynamic parameters in the testes were significantly reduced. In particular, the mean maximum blood flow rate in the testicular arteries decreased to (15.6±1.0) cm/s against (18.5±1.5) cm/s, which led to a decrease in testicular volume to 15.5±1.3) cm3 versus (17.6±1.0) cm^3 in the control. The study of testicular bioptates' histological specimens shows a decrease to (160.5±12.7) μm against (196.9±10.3) μm in the diameters of convoluted seminiferous tubules, the own membrane of which is significantly thickened, and in some of them cells of the epithelium spermatogenesis were not determined. Reduced were the volume of interstitial endocrinocyte nuclei to (72.5±3.6) $μm^3$ against (90.2±1.5) $μm^3$, and the testosterone level – to (370.0±9.0) ng/dl against (590.0±30.0) ng / dl in the blood.

Significant ultrastructural changes in the testes with thickening of the spermatogenic epithelium basal membrane, vacuolation of the myoid cells' cytoplasm, supported epitheliocytes and intestinal endocrinocytes with reduction of mitochondrial crista were revealed. In the connective apparatus of epitheliocytes, the cytosolic membranes are approximated and cisterns of the endoplasmic reticulum are expanded [7, 8].

In the ejaculate of men under these conditions, the concentration of spermatozoa was reduced to (18.20±1.50) million/ml, their total number – to (64.06±5.4) million/ml, against (71.1±3.6) million/ml and (190.15±15.320) million/ml in the control [5, 6].

Conclusions

1. In benign hyperplasia, the volume of the prostate increases to (51.2±2.0) cm^3 against (33.4±1.0) cm^3, and the peak blood flow rate decreases to 7.70 cm/s against 16.50 cm/s in the control, and volumetric blood flow – up to 0.03 l/min against 0.06 l/min. There is an increase to 56.6 % in the number of stromal components and a decrease to 43.5 % – in the glandular component with a decrease in the height of the glandular epithelium.

2. In mature men with benign prostatic hyperplasia, the volume of the testis decreases to (15.5±1.3) cm^3 against (17.6±1.0) cm^3 in the control, and the diameter of the convoluted seminiferous tubules – to (170.3±10.1) μm versus (190.60±11.20) μm, there is a reduction in the layers of spermatogenic epithelial cells.

3. The maximum mean blood flow rate in the testicular artery under these conditions is reduced to (15.6±1.0) cm/s, and the volumetric blood flow – to (8.7±1.2) ml / s against (18.5±1.3) cm/s and (10.6±1.0) ml/s in the control.

4. In the ejaculate of men, the spermatozoa concentration decreases to (18.20±11.50) million/ml, the number of morphologically normal spermatozoa – up to 39.5 % against (71.20±3.60) million/ml and 64.2 % in the control. The number of live spermatozoa decreases to 56.1 % vs. 65.8 % and the number of progressive mobile spermatozoa decreases to 15.6 % vs. 27.5 %. In the blood of men in this group, testosterone levels are reduced to (370.0±9.0) ng/dL against (590.0±3.0) ng/dL in the control.

Prospects for further research lie in the correction of spermatogenesis in infertile men using phytotherapy.

References

1. Bazalytska SV. Osoblyvosti ekspresii proteinu Claudin 11 ta stan hematotestykuliarnoho barieru pry riznykh formakh cholovichoyi neplidnosti. Svit medytsyny ta biolohii. 2015; 2(49):79–82. [in Ukrainian]

2. Bazalytska SV. Cholovicha neplidnist v Ukrayini: osoblyvosti pato- i morfohenezu [monohrafiia]. Kyiv: Chetverta khvylia; 2016. 262 s. [in Ukrainian]

3. Boiko MI, Chornokulskyi IS. Laboratorne doslidzhennia eiakuliatu v prohnozi uspishnosti tsykliv DRT pry cholovichiy neplidnosti. Urolohiya. 2013; 2(65):52–53. [in Ukrainian]

4. Bragina EE, Bocharova EN. Kolichestvennoe elektronno-mikroskopicheskoe issledovanie spermatozoidov pri diagnostike muzhskogo besplodiya. Andrologiya i genitalnaya khirurgiya. 2014; 15(1):41–50. [in Russian]

5. Hotiur OI. Hemodynamycheskiye izmeneniya v yaichke i ikh vliyanye na spermatogenez v usloviyakh levostoronnego varikotsele. Nauchnoye obozrenie. 2013; 9:461–464. [in Russian]

6. Hrytsuliak BV, Hrytsuliak VB, Hotiur OI, Dolynko NP, Polyvkan MI. Ultrastruktura hemokapiliariv ta vlasnoyi obolonky zvyvystykh simianykh trubochok yaiechka u cholovikiv zriloho ta pokhyloho viku. Halytskyi likarskyi visnyk. 2013; 2(20): 39–41. [in Ukrainian]

7. Chaikovskyi YuB, Polyvkan MI. Zminy hemodynamiky ta spermatohenezu u neoperovanykh cholovikiv v umovakh kosoi pakhvynnoi hryzhi. Svit medytsyny ta biolohii. 2017; 1(59): 87–89. [in Ukrainian]

8. Chornokulskyi IS, Chaikovskyi YuB, Boiko MI, Bazalytska SV. Morfolohichni osoblyvosti cholovichykh eiakulyovanykh spermatozoyidiv v normi ta pry neplidnosti. Svit medytsyny ta biolohii. 2013; 4(42):108–115. [in Ukrainian]

9. Schill WB, Comhaire FN, Hargreave TB. Andrology for the Clinician. Springer-Verlag Berlin Heiderberg; 2011. 800 p.

Стаття надійшла 13.03.2020 р.