

THE INCREASE OF ARTERIAL HEMODYNAMICS IN PATIENTS WITH VARICOCELE AND INFERTILITY

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The aim of the investigation was to develop the technique of effective and pathologically reasonable management of infertility in male patients with varicocele.

Materials and Methods. The research was based on the results of clinical observations of 865 patients with varicocele aged 18–39 years, classified into two groups depending on the presence or absence of spermatogenesis disturbances. The pattern of changes in hemodynamic indices in different periods after varicocele surgical treatment was studied in 135 patients. Ejaculate was examined in accordance with WHO laboratory manual for the examination and processing of human semen (1987). Hemodynamic condition in scrotal organs was assessed by ultrasound on “Aloka SSD-3500” and “Aloka SSD-4000” (Japan) using linear probe 7.5 MHz. The spermatogenesis condition in infertility was evaluated by morphological examination of the material obtained by testicular biopsy.

Results. The analysis of the surgical treatment results of 135 patients showed the improvement of arterial testicular blood supply in 97 patients (71.8%). The rest 38 patients (28.2%) had no changes in arterial blood supply, but in some cases (9 patients) there was insignificant increase of arterial testicular blood supply within the first month after the surgery. The developed operational procedure for varicocele included the superior testicular vein ligation, which was followed by the ligation of a. hypogastrica inferior in 93 patients. The findings suggest great efficiency of the technique. The recovery of ejaculate parameters takes far less time compared to standard varicocelectomy.

Key words: varicocele; testicular hemodynamics; spermatogenesis impairment.

Pathogenesis of spermatogenesis disturbance in varix dilatation of the funicle is not completely studied, though evidence in favor of ischemic factor can be found. Impairment of testicle parenchyma blood supply detrimentally affects spermatogenesis, because spermatogenic epithelium is highly sensitive to ischemia. It is estimated, that prolonged hypoxia results in aspermatogenesis, hypoxic aspermatogenesis being an autoimmune process.

One way of solving the problem of infertility treatment in varicocele is a surgical one, consisting of elimination of venous hypertension. To reach the goal a lot of different techniques has been offered [1–7], the results of a surgical correction of varicele, however, are rather ambiguous [8]. Thus, Mordel N. et al. [9] give in their work a review of 35-year research on the treatment of 5471 patients. It has been noted, that normalization of ejaculate values after surgical treatment of varicocele occurred in 8–23% of cases, pregnancy was noted in 0–63% of cases (36% on average), while improvement was observed in 0–92% (57% on average). A number of specialists give rather a sceptical assessment of the efficiency of surgical intervention in varicocele, believing it to be only an attempt to solve a serious problem by a simple way [10].

The reason of such low results of infertility surgical treatment in varicocele is underestimation of mechanisms

of spermogenesis disorder development in these patients. Complex experimental clinical evaluation of blood flow condition of the scrotum organs (testicles and epididymes) showed, that in venous hypertension its complicated alteration takes place, including at early stages of process development addition of microcirculation of the autoregulatory veno-arterial reaction to the post-capillary block, manifesting itself by a spasm of the bloodstream arterial segment [11, 12]. Surgical correction of varicocele solves the problem of venous hypertension only, while arterial hemodynamics in the testicle remains damaged.

The aim of investigation was to devise a technique of effective and pathogenically grounded management of infertility in male patients with varicocele.

Materials and Methods. The work is based on the analysis of clinical observations of 865 patients with varix dilatation of the funicle at the age of 18–39, which underwent examination and treatment from 1983 to January 2010 in the urological units of Nizhny Novgorod Regional Clinical Hospital after Semashko — a teaching base of the Urological Department of Nizhny Novgorod State Medical Academy (Russia). According to the clinical course of varicocele patients were divided into two groups depending on the presence or absence of spermatogenesis disturbances. The 1st group (n=584) consisted of the patients

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with varicocele and infertility, the 2nd one (n=281) included males with varicocele and normal spermatogenesis, confirmed by laboratory findings and availability of healthy children.

Ejaculate was investigated according to the WHO Guidelines for laboratory examination of human semen and its interaction with cervical mucus (1987). Hemodynamics condition in scrotal organs was assessed by ultrasound using "Aloka SSD-3500" and "AlokaSSD-4000" ultrasound systems with a linear 7.5 MHz probe. Spermatogenesis in infertility was evaluated by morphological examination of the material, obtained by testicular biopsy.

Results and Discussion. The pattern of hemodynamic changes in different terms after the surgical treatment of varicocele was studied in 135 men. In 97 of 135 patients (71.8%) improvement of arterial flow to the testicles was noted. In the rest 38 men (28.2%) changes in arterial flow did not occur, though in some cases (9 patients) insignificant increase of arterial blood flow to the testis during the first month after the operation was observed.

In 97 patients, responded to the surgery, dynamics of the arterial blood flow restoration in the post-operative period and comparative characteristic of the blood supply restoration rate were studied. It was estimated that restoration of blood flow parameters takes about half a year. And the intensity of changes and the terms of vascular hemodynamics improvement depend on the duration of the disease and the character of alterations in the microcirculatory bloodstream of the testicular parenchyma rather than on the degree of varix dilatation of the funicle.

The effect of varicocele surgical repair on spermatogenesis was investigated in patients with original pathospermia (n=270) and in patients with normal sperm indices (n=144). It was noted, that values of spermogram after surgical treatment of varicocele changed in both groups. However, in patients with normal spermogram alterations of qualitative ejaculate values in the majority of cases became better, while in those with pathological changes of spermogram ejaculate indices did not always improve.

In patients with varicocele, having normal values of spermogram, statistically significant improvement of ejaculate indices after operative treatment was noted in 91 patients of 144 (63.2%), in 31 (21.5%) some worsening of both concentration and sperm motility was found, in other cases there were no changes in ejaculate values. It is notable that after the operation mean concentration of sperm remained at the same level. Thus, if sperm concentration in 3 months after the operation reduced by 4.1% (up to 79.80 ± 0.50 mln/ml), it enlarged by 0.5% (up to 83.60 ± 0.39 mln/ml) of the original value (83.20 ± 0.34 mln/ml) in 6 months.

Varicolectomy causes the largest effect on motility and morphology of sperm. The quantity of spermatozoons with normal motility in 3 months after the operation reduced by 3.5% (up to $60.40 \pm 0.32\%$), but by the 6th month it increased by 3.6% ($64.90 \pm 0.36\%$) of the original value ($62.60 \pm 0.40\%$). The quantity of spermatozoons with low motility after the operative treatment dropped by the 3rd month by 3.3% (up to $11.84 \pm 0.06\%$), but in 6 months it grew by 9.3% (up to

$13.50 \pm 0.12\%$) of the original figure ($12.24 \pm 0.05\%$). The concentration of immobile spermatozoons after 3 months elevated by 10.6% (up to $20.03 \pm 0.22\%$), and lowered by 8.4% (up to $16.40 \pm 0.12\%$) of the original value ($17.90 \pm 0.12\%$) already by the 6th month.

The concentration of morphologically normal spermatozoons in 3 months after the operation decreased by 8.7% (up to $70.0 \pm 0.74\%$), and grew in 6 months by 1.3% (up to $77.40 \pm 0.66\%$) of the original value ($76.70 \pm 0.44\%$). The number of spermatozoons with pathological heads in 3 months fell by 8.3% (up to $11.10 \pm 0.14\%$), and in 6 months — by 16.5% (up to $10.10 \pm 0.13\%$) of the original value ($12.10 \pm 0.16\%$). The quantity of spermatozoons with cervical pathology in 3 months after surgery became less by 3.6% (up to $7.06 \pm 0.07\%$), but in 6 months — by 8.5% (up to 6.70 ± 0.06) of the original value ($7.32 \pm 0.07\%$). Concentration of spermatozoons with tail pathology in 3 months after the operation reduced by 10.6% (up to $5.25 \pm 0.08\%$) in 6 months — by 15.3% (up to $4.97 \pm 0.04\%$) of the original figure ($5.87 \pm 0.07\%$).

Thus, varicolectomy leads to the progressive increase of the number of the morphologically normal forms of sperm cells. However, though a percentage of morphologically normal sperm cells grows by 4.1% in 6 months after surgery, it occurs at the expense of the reduction of the number of spermatozoons with the cervical and tail pathology only (by 3 and 1.1% respectively).

Quite a different situation is observed, when analyzing the dynamics of spermogram values in patients with varicocele and infertility. The operative treatment of varicocele was also accompanied by the changes in the main values of ejaculate in the majority of patients, but the pattern of these alterations was different. Thus, statistically significant improvement of ejaculate indices was noted only in 138 of 270 patients (51.3%), in 64 patients (23.6%) there were no changes at all, while in 68 (25.1%) patients statistically significant worsening of the main ejaculate values took place.

As all operations on varicocele in patients with infertility were accompanied by testicle biopsy, we got an opportunity to analyze the character of clinical response on the part of spermatogenesis to varicolectomy performed depending on the morphological changes in the testis.

In those cases, when in response to the operation on varicocele there were no changes in the main parameters of ejaculate, orchis biopsy revealed alterations characteristic of chronic inflammatory process. In all patients marked impairment of spermatogenesis was noted, the basal membrane of convoluted tubules was thickened, and in some cases it was fiberless. The number of Sertoli cells was reduced and, additionally, in some cases dystrophic changes in the form of vacuole and sometimes balloon dystrophy in their cytoplasm were noted. In the testis capillary walls changes were characterized by fibrosis development, and in separate cases, in addition to fibrinosis, fibrinoid swelling was observed. Interstitial testicular tissue in the majority of men was intensively thickened and fibrotized. The morphological testicular changes revealed characterize chronic autoimmune inflammatory process which cannot be reversed.

In the group of patients, in which there was worsening of spermogram values after the operative treatment of varicocele (68 males), changes in the testis tissue took mainly the form of microcirculatory bloodstream reconstruction, characterized by the prevalence of moderate diameter increase of intratesticular veins. It was combined with the higher density of venous vessel arrangement and hypertrophy of the muscular layer of small arteries. The inner lumen of these vessels was not also identical everywhere, besides, morphological signs of spasm in the form of the folded internal contour of endothelium, its longitudinal disorientation, as well as corrugation and destruction of the basal membrane with occasional plasmatic impregnation of the vessel wall were revealed.

Changes in spermatogenesis were insignificant and were characterized mainly by disarranged cellular structures of the spermatogenous epithelium. In the cytoplasm of spermatocytes and spermatogones vacuole dystrophy and moderate fibrosis in the membrane of seminiferous tubules were observed in some patients. Thus, changes

in the testis parenchyma in this group of patients can be evaluated as reversible, though elimination of venous hypertension and spasm of the arterial component of the testicle microcirculatory bloodstream result in aggravation of hypoxia in the post-operative period and development of serious impairment of spermatogenesis.

To prove our conclusions concerning the mechanism of spermatogenesis depression after the operation on varicocele investigation was carried out. It included 93 patients with varicocele in whom the operation of superior testicular vein ligation according to Ivanissevich was complemented by ligation of a. hypogastrica inferior in order to increase the arterial flow through the cremasteric artery.

For the first time we learned about the development of surgical techniques of intensifying arterial blood inflow to the testicle as a way of its blood supply improvement for prevention and management of hypogonadism from the work of Y.P. Melman et al. [13]. The data obtained served as a basis for searching the methods of testicle revascularization in case of their blood supply impairment.

Table 1

Values of hemodynamics in patients with varicocele in 3 and 6 months after operative treatment

Indices	Control group (n=97) – Ivanissevich operation			Main group (n=93) – Ivanissevich operation with arterialization		
	before operation	3 months	6 months	before operation	3 months	6 months
<i>Left testicle</i>						
Cremasteric artery:						
PSF, cm/s	11.31±0.61 —	13.30±0.47 <0.005	13.8±0.35 <0.005	11.06±0.41 —	12.04±0.30 <0.05	13.12±0.33 <0.005
TDF, cm/s	4.09±0.19 —	5.15±0.19 <0.005	5.31±0.17 <0.001	4.12±0.15 —	4.84±0.14 <0.05	5.81±0.17 <0.001
RI	0.65±0.01	0.58±0.01 <0.005	0.58±0.01 <0.005	0.64±0.01 —	0.62±0.01 <0.05	0.57±0.01 <0.005
Central artery:						
PSF, cm/s	6.83±0.39 —	8.36±0.36 <0.005	8.59±0.34 <0.005	6.99±0.31 —	8.64±0.28 <0.05	8.92±0.29 <0.005
TDF, cm/s	3.32±0.15 —	3.72±0.14 <0.05	3.78±0.14 <0.05	3.31±0.11 —	3.78±0.12 <0.005	3.98±0.12 <0.001
RI	0.62±0.02	0.56±0.01 <0.005	0.55±0.13 <0.005	0.60±0.01 —	0.54±0.01 >0.05	0.53±0.01 <0.05
<i>Right testicle</i>						
Cremasteric artery:						
PSF, cm/s	11.91±0.66 —	13.26±0.38 <0.05	13.43±0.39 <0.05	12.05±0.41 —	12.36±0.28 <0.05	9.97±0.24 <0.005
TDF, cm/s	3.82±0.16 -	4.74±0.15 <0.001	4.83±0.15 <0.001	3.91±0.12 —	4.28±0.10 <0.05	4.62±0.13 <0.001
RI	0.67±0.02 —	0.62±0.01 <0.05	0.60±0.01 <0.005	0.65±0.01 —	0.65±0.01 >0.05	0.59±0.001 <0.005
Central artery:						
PSF, cm/s	7.43±0.45 —	9.17±0.43 <0.05	9.28±0.43 <0.005	7.11±0.30 —	9.74±0.24 <0.05	9.58±0.23 <0.005
TDF, cm/s	3.49±0.17 —	4.17±0.16 <0.005	4.28±0.16 <0.005	3.25±0.12 —	3.66±0.11 <0.05	4.32±0.12 <0.001
RI	0.61±0.01 —	0.56±0.01 <0.005	0.53±0.01 <0.005	0.59±0.01 —	0.58±0.01 >0.05	0.53±0.01 <0.005

Notes: statistical significance of value differences is indicated for the groups before and after the operation

Being rather technically easy, the operation on the inferior epigastric artery ligation, made by Y.M. Kudryavtzev et al. [14] in patients with infertility, resulted in significant improvement of spermatogenesis in 5 patients of 6 already in a month. That is why to correct the deficiency of blood flow to the testicle, occurring in varicocele, the operation of superior testicular vein ligation was complemented by the ligation of the inferior epigastric artery on the side of varicocele.

Only one of 93 patients operated on according to this method had a complication in the early post-operative period: arterial bleeding because of loosening of the ligature. Bleeding was arrested by resection of the vessel.

Dynamics of the arterial bloodstream reconstruction in the post-operative period was studied and comparative characteristic of blood supply reconstruction rate was made in all 93 patients (the main group). To make it clear, the results of the treatment were compared with the hemodynamic data of the patients (97 males) undergone Ivanissevich operation only and obtained a positive

response (control group) (Table 1). It should be noted, that Ivanissevich operation with arterialization of the testicle by inferior epigastric artery ligation always gave a positive response to the operation on the part of the hemodynamic testicle bloodstream and spermatogenesis, and it occurred much earlier than after the Ivanissevich operation only.

Thus, in the main group in the left testicle peak systolic flow (PSF) in cremasteric artery increased by 8.1% in 3 months after the operation, and by 8.8% of the original value in 6 months. Terminal diastolic flow (TDF) increased by 10.2% in 3 months after the operation, and by 30.6% in 6 months. Resistance index (RI) in the cremasteric artery dropped by 3.1% in 3 months after the operation, and by 10.9% of the original value in 6 months. PSF in the central artery rose by 13.6% in 3 months, and by 14.9 of the original value in 6 months. TDF in the central artery grew by 19.4% in 3 months, and in 6 months by 22.8% of the original value. RI reduced by 3.5% in 3 months and in 6 months after the operation — by 5.2% of the original value.

So, in patients with varicocele significant improvement

Table 2

Dynamics of ejaculate indices in patients with varicocele after operative treatment

Ejaculate index	Control group (n=97) — Ivanissevich operation			Main group (n=93) — Ivanissevich operation with arterialization			
	before operation	3 months	6 months	before operation	3 months	6 months	Norm
Volume, ml	3.01±0.10 —	3.06±0.09 >0.05	7.41±0.04 >0.05	3.0±0.14 —	3.2 ±0.20 >0.05	3.66±0.17 p ₁ <0.005 p ₂ >0.05	3.26±0.41
pH	7.41±0.03 —	7.43 ±0.04 >0.05	7.31±1.44 >0.05	7.45±0.04 —	7.52±0.04 >0.05	7.41±0.04 p ₁ >0.05 p ₂ >0.05	7.39± 0.04
Spermatozoon concentration, mln/ml	15.1 ±0.37 —	20.5 ±0.32 <0.001	41.61±1.48 <0.001	14.9±0.45 —	24.76±0.41 <0.001	58.70±1.44 p ₁ <0.001 p ₂ >0.05	45.61±6.17
Spermatozoon normal motility, %	22.4 ±0.29 —	41.21±0.96 <0.001	40.9±0.37 <0.001	22.76±0.33 —	50.47±1.81 <0.001	71.81±1.48 p ₁ <0.001 p ₂ >0.05	69.70±3.14
Spermatozoon, low motility, %	16.96±0.29 —	15.45±0.29 <0.005	24.35±0.20 <0.001	17.62±15.2 —	15.2±0.52 <0.005	12.9±0.37 p ₁ <0.001 p ₂ >0.05	15.31±1.61
Immobile spermatozoons, %	60.08±0.93 —	43.2±0.55 <0.001	34.85±1.82 <0.001	59.57±2.33 —	34.2±3.42 <0.001	15.35±0.20 p ₁ <0.001 p ₂ >0.05	15.01±2.83
Morphologically normal spermatozoons, %	47.6±0.69 —	48.6±1.08 >0.05	52.65±0.23 <0.001	47.5±1.42 —	62.25±0.86 <0.001	71.8±1.82 p ₁ <0.001 p ₂ <0.005	67.20±3.01
Spermatozoons with head pathology, %	29.53±0.28 —	27.52±0.32 <0.001	22.35±0.23 <0.005	19.24±0.63 —	15.95±0.47 <0.005	12.65±0.23 p ₁ <0.001 p ₂ >0.05	16.90±1.71
Spermatozoons with cervical pathology, %	10.51±0.25 —	9.46±0.24 <0.005	13.31±0.38 <0.001	10.71±0.56 —	9.3±0.39 <0.05	8.35±0.23 p ₁ <0.005 p ₂ >0.05	4.21±1.02
Spermatozoons with tail pathology, %	12.35±0.19 —	9.87±0.26 <0.001	11.69±0.22 <0.001	12.14±0.31 —	9.5±0.27 <0.001	7.20±0.38 p ₁ <0.001 p ₂ >0.05	7.53±1.15

Notes: statistical significance of value differences is indicated for the groups before and after the operation; p₁ — before the operation and in 6 months; p₂ — within the group after the operation, 6 months, and the norm

of hemodynamic values was found independently on the operation performed. However, taking into account the ischemic genesis of infertility in varicocele the time of blood supply reconstruction after the operation is of crucial importance. If in the first months after varicocelectomy hemodynamic indices improve insignificantly or in a number of cases become even a bit worse, the combination of the superior testicular vein and inferior epigastric artery ligation gives stable improvement of testis blood supply already within the first days.

Examination of ejaculate in patients with varicocele after Ivanissevich operation with orchis arterializations (the main group) was performed 3 and 6 weeks later (Table 2). It should be mentioned, that a positive dynamics was seen in all patients.

Comparison of statistically processed ejaculate values of the main and control groups (patients with a positive response to the operation) showed much better results in terms of statistical significance after the operation with orchis arterializations. If the ejaculate volume and its pH did not undergo any changes, statistically significant response of the main spermogram parameters appeared already in 3 months. Spermatozoon concentration almost doubled — from 14.9 ± 0.45 mln/ml to 24.76 ± 0.41 mln/ml, and in 6 months this value was almost similar to the value of healthy fertile men ($p > 0.05$) and amounted to 58.70 ± 1.44 mln/ml. The number of spermatozoons with normal motility became almost twice as much in 3 months, and in 6 months it approached to the values of healthy men. Indices characterizing spermatozoon morphology also changed. Already in 3 months the number of spermatozoons with the normal structure considerably increased, and in half a year it practically was near the norm.

The obtained results of ejaculate parameter changes in male patients with varicocele and infertility after Ivanissevich operation with orchis arterialization on the side of varicocele by inferior epigastric artery ligation speak of a great efficacy of this management technique. The recovery of the parameters takes far less time than in conventional varicocelectomy. Positive dynamics of the main ejaculate values is noted already in 3 months, and in half a year they are practically approaching the normal ones.

Conclusion. Normalization of testicular blood supply rather than elimination of venous hypotension must be the aim of treating infertility due to varicocele. In those cases when due to compensatory spasm of the arterial link of microcirculatory bloodstream a sort of blood pressure balance is reached in the testicle, a simple removal of venous hypertension by ligation of superior testicular veins leads to testis ischemia, as arteries remain for some time in the state of spasm. Terms of hemodynamics recovery vary, but it is well known, that even a short-term ischemia is fatal for spermatogenesis. If there are changes of arterial bloodstream in the form of spasm in patients with varicocele and infertility, elimination of venous hypertension must be accompanied by reconstruction of arterial hemodynamics.

It can be done either by involving conservative therapy in the management process, or by creating intensive inflow of arterial blood to the testicle ligating inferior epigastric artery.

Morphological investigations performed showed that the result of varicocele operative treatment to improve spermatogenesis is directly related with the morphological changes in the testis parenchyma. Therefore, testicular biopsy in infertility and varicocele must be mandatory. And only having obtained morphological findings the effect of varicocelectomy can be predicted for every individual patient. In case of irreversible changes in the testicular parenchyma the operation will be of purely cosmetic character.

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