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Varicocele in Men: The Problem of Male Infertility

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Abstract: Demographic problems in Uzbekistan require paying more attention to reproductive health of adolescents. WHO reports 50% contribution of male factor in infertile couples. Among the reasons causing male infertility varicocele can be emphasized. Numerous of long-term researches are dedicated to male infertility in adults. Far less researches of varicocele in kids and adolescents can be found. That could be connected with particularity of diagnostic and treatment. Varicocele influence on spermatogenesis and surgery efficiency are still discussed and researched. Materials and methods. 500 patients with varicocele underwent surgery for last 5 years in BRMMC of Urology. Diagnosis was based on physical examination, ultrasound and Doppler investigation. Left-sided varicocele was in 89% of cases, right-sided in 1%, two-sided in 10%. Spermatogenesis status was determined due to WHO recommendations. In a group of 200 adolescents after parental permission ejaculate analyses was taken. Age varied from 16 to 18. Statistic analyses was used. Results. Mean level of main ejaculate characteristics was lower than normally. After the surgery sperm cells concentration increased meanly from 35 to 61 mln/ml, quantity of alive cells meanly increased from 70% to 77%. “A” category sperm cells improved meanly from 20% to 50%.

Conclusions. Varicocele affects spermatogenesis, can lead to infertility. In adults, significant changes in spermatogenesis in most cases, surgery gives positive results.

Keywords: varicocele, male infertility, andrology, spermatogenesis.

According to the Ministry of Health of the Republic of Uzbekistan. in Uzbekistan, more than 40,000 men suffer from infertility, among women these figures are much higher - from 40,000 to 50,000. Unfortunately, an andrological service (similar to women's consultations) has not yet been formed in our country, and the data on the spread of male infertility are very approximate and underestimated .

According to WHO, the etiology of male infertility is currently represented by almost 30 causes. At the same time, the idiopathic form accounts for up to 16-25% of all cases. It is believed that varicocele is the cause of infertility in 9-40% of patients. Such large differences in these indicators testify to the debatability of this provision. The prevalence of varicocele among adolescents aged 16-24 reaches 20%. Early detection of varicocele makes it possible to correct impaired fertility and preserve reproductive function in childbearing age. Teenagers, like future fathers, socially represent a demographic potential. Therefore, this disease attracts increased attention not only from medical, but also from socio-demographic positions.

The literature debates the degree of effectiveness of surgical correction of varicocele, as well as the impact of this disease on the level of spermatogenesis and ejaculate fertility in adults. In clinical studies, there are diametrically opposed points of view: some authors believe that varicocele does not affect the fertility of the ejaculate, others argue that with varicocele, the

normal process of maturation of the spermatogenic epithelium is inhibited. The latter statement is substantiated by a large number of experimental studies: the creation of an artificial varicocele in rats caused a negative effect on spermatogenesis even with short-term testicular ischemia. In the convoluted seminiferous tubules, structural disorders of the spermatogenic epithelium occur, the activity of enzymes involved in the transformation of androgens changes. Ischemia leads to an increase in the concentration of reactive oxygen species in cells and oxidative stress, which is noted in patients with varicocele.

Clinical studies conducted in groups of adolescents aged 15-17 convincingly confirm the data on the wide spread of varicocele at this age: from 9 to 25%. However, these works do not indicate specific parameters of spermatogenesis, the authors limit themselves to a general description of the latter (depressed or not impaired), do not provide statistical materials, and there are no objective data on the dynamics of the state of spermatogenesis in this group of patients. Determining the level of hormones, the size of the testicles and Dopplerography of the veins of the spermatic cord do not allow a full assessment of the reproductive function of the testicles in adolescents.

A number of authors indicate that when examining young patients with varicocele in 12% of cases, testicular atrophy is found on the side of the lesion. At the same time, testicular dysfunction, determined by the study of the hormonal profile, is recorded in these young men. Studies conducted by WHO have established that spermatogenesis at a fertile level is possible only in testicles of normal size, i.e. with a volume of each testicle of at least 15 ml.

In adolescents, if it is impossible to obtain an ejaculate, hormones are determined in the peripheral blood and in the testicular veins. A high correlation was found between the size of the testis and the content of follicle-stimulating hormone (FSH) in the peripheral blood. In clinical studies, an increase in the levels of FSH, luteinizing hormone (LH) and prolactin in peripheral blood has been confirmed. When determining androgens in the veins of the spermatic cord, a decrease in the level of testosterone was found. A comparative study of the concentration of LH in patients with varicocele in the control group did not reveal significant differences. In boys aged 15-16 years with stage II-III varicocele, there is a tendency to increase the excretion of dehydroepiandrosterone. At the same time, they have a decrease in the excretion of 11 and 17-hydroxycorticosteroids and androstenediol.

It has been established that in boys at the beginning of puberty, there is a rapid rise in LH in the blood plasma, which later settles at a certain level, while FSH rises slowly until the end of puberty, reaching the value of adult men. In healthy men, the concentration of gonadotropins does not change significantly with age. Only after 70 years there is a slight increase in LH in blood plasma without significant changes in the level of FSH.

It is known that varicocele is found in early childhood. At the same time, the influence of the duration of the existence of varicocele on spermatogenesis has not been studied at all. So far, varicocele in children and adolescents is discovered more often by chance, when it manifests itself with already noticeable varicose veins or pain. However, it is not always possible to assess the state of spermatogenesis in them. This opportunity appears later, at the age of 16-18 years. There are single works that give a general description of the state of spermatogenesis in young men, but without highlighting individual parameters of the ejaculate, which is clearly not enough. The subject of discussion also remains the question of the time of surgical intervention in case of detection of varicocele in adolescents in order to prevent possible infertility.

Thus, there are different points of view on the problem of varicocele in adults and adolescents. The controversial nature of the issues raised was the basis for a comparative study of the state of spermatogenesis in different age groups before and at different times after surgery for varicocele and, on this basis, to express their point of view on this social problem.

Materials and methods of research

Over the past 5 years, more than 500 patients with varicocele have been examined at the Research Institute of Urology. The diagnosis was established on the basis of palpation examination, ultrasound of the scrotum and Doppler sonography. Left-sided lesion occurred in 87% of cases, right-sided in 2% and bilateral varicocele in 11% of cases.

The state of spermatogenesis was assessed according to the WHO recommendations. Ultrasound and dopplerography were performed according to standard methods. Operational aid was performed according to the Ivanisevich method or sclerotherapy was used. Biochemical parameters of sperm were determined by the methods described by us earlier.

In the group examined, 226 adolescents (with the consent of the parents of each patient) received ejaculate. Obtaining ejaculate from adolescents was carried out by the WHO-accepted method of masturbation and in no case was accompanied by a refusal and did not cause them any psychological discomfort. All of them have already had this experience for several years. The age of the patients ranged from 16 to 18 years. This age group was divided into 4 subgroups. Statistical processing of the material by the Mann-Whitney method, used for any distribution, was carried out.

Table 1. Effect of varicocele on the function of the male reproductive system

Indicators	Age (years)						WHO standards
	16-18	16	17	18	16,5	26	
Volume(ml)	1,9 ± 0,7	2,1 ± 0,1	2,1 ± 0,1	2,6 ± 0,2	2,2 ± 1,2	3,8 ± 1,5	2-6
Concentration (ppm/ml)	52 ± 1,9	56 ± 5,1	55 ± 4,7	62 ± 4,7	53 ± 21,6	62,9 ± 15	over20
active mobility	11 ± 0,4	12 ± 1,2	11,8 ± 1,0	12,2 ± 1,0	9,8 ± 5,8	10,3 ± 5,2	Over 25
Low mobility	29 ± 0,7	30 ± 1,5	30 ± 1,7	31 ± 1,5	33,5 ± 7,1	25,6 ± 9,9	Over 25
Normal morphology (%)	38 ± 0,8	40 ± 1,6	40 ± 1,6	42 ± 1,4	41 ± 7,0	37 ± 8,2	More than50
Spermatogenesis cells (%)	4,2 ± 0,2	4,4 ± 0,3	3,4 ± 0,4	3,9 ± 0,4	3,8 ± 2,1	2,9 ± 1,2	1-2
Citric acid (mM/ml)	27,2 ±1,1	30,6 ± 3,8	28,2 ± 2,9	35,5 ± 4,9	33 ± 17,5		Over 53 in ejaculate

Results and discussion

Table 1 shows the results of the main parameters of the ejaculate, as well as the concentration of citrate, a marker of the functional activity of the prostate gland. It has been established that in adolescents with varicocele, the level of such parameters as ejaculate volume, active sperm motility, normal sperm morphology, the number of spermatogenesis cells is below the normal fertility limit, including the content of citric acid. Taking into account the WHO standards, it is important to note that those parameters that determine the level of ejaculate fertility, sperm motility and morphology turned out to be reduced. In the group of adolescents with reflux into the testicular veins, the parameters of spermatogenesis were at the level similar to those in the group of the same age, i.e. 16 years.

Table 2 shows the results of a study of the ejaculate of adult men with varicocele for a comparative analysis before and after surgical correction. A higher scatter of digital indicators of all parameters of the ejaculate was noted. The value of each parameter before the operation was close to the values of the same parameters in adolescents. After the operation, the level of sperm motility did not change, the number of normal forms of germ cells did not increase.

Table 2. Status of spermatogenesis in adult patients with varicocele before and after surgery

indicators	before surgery	after surgery
Number of patients (n)	132	44
Age (years)	27,3 ± 0,5	29,1 ± 0,8
Ejaculate volume (ml)	3,5 ± 0,1	4,1 ± 0,2
Sperm concentration (million/ml)	61,3 ± 3,0	48,8 ± 6,1
Live spermatozoa (%)	63,9 ± 1,6	63,7 ± 3,3
Actively motile spermatozoa (%)	9,6 ± 0,5	9,3 ± 1,2
Sedentary (%)	23,4 ± 1,1	23,7 ± 2,0
Normal morphology (%)	36,1 ± 1,0	36,2 ± 2,3
Spermatogenesis cells (%)	2,4 ± 0,1	2,2 ± 0,2

Table 3 presents the results assessing the state of spermatogenesis in adolescents aged 16-18 years 6-24 months after surgery. The results obtained indicate the normal state of the parameters of the ejaculate, corresponding to the WHO standards for adults.

Table 3. The state of spermatogenesis and the function of the gonads in adolescents aged 16-18 years after surgery for varicocele

Indicators	group with varicocele after surgery	WHO standards
Ejaculate volume (ml)	1,4 ± 0,8	2.0-6.0
Sperm concentration (million/ml)	61,0 ± 33,0	over 20
Live spermatozoa (%)	77,0 ± 4,0	more than 50
Actively motile spermatozoa (%)	36,0 ± 14,0	over 25
Sedentary (%)	23,0 ± 6,0	over 25
Normal forms (%)	37,0 ± 11,0	more than 50
Spermatogenesis cells (%)	2,0 ± 0,3	1-2
Fructose (mM/l)	13,0 ± 4,3	over 13.0
Citric acid (mM/l)	13,9 ± 5,3	over 53.0
Zinc ions (mM/l)	0,8 ± 0,3	over 2.0

The study of the biochemical characteristics of the ejaculate, which reveal the function of the gonads before and after the operation, showed that in both groups the level of indicators did not differ significantly, but the function of the prostate gland, determined by the concentration of citric acid and zinc ions, in adolescents remained significantly below the level adopted for adults. Perhaps this is due to irregular sex life. However, one cannot exclude the fact that impaired hemodynamics in varicocele can capture the area of blood supply to the additional gonads, thereby having a negative effect on their secretory function.

Thus, the postoperative analysis of the ejaculate in adolescents shows the beneficial effect of the correction of varicocele, which made it possible to raise the preoperative level of subfertility above the lower physiological limit of fertility.

Less revealing, in comparison with the results of adolescents, are the data obtained in the group of adult men with varicocele. The data in Table 2 indicate that the postoperative state of the main parameters of the ejaculate does not undergo significant positive changes. The absence of the expected positive dynamics, probably to a greater extent, is based on the low level of ejaculate indicators at the time of the patient's admission to the clinic, which allows us to draw certain conclusions. However, despite the absence of a group-wide effect, in some cases individual results were more encouraging.

In addition to biochemical parameters, in a separate group of adult men with varicocele, the protein composition of the ejaculate was studied, in which attention was paid to lactoferrin. This

protein has an antioxidant function and responds to changes in the oxygenation of the ejaculate. It was found that the level of lactoferrin before surgery was lower than in healthy sperm donors. After surgery, this level dropped significantly compared to the preoperative period, which probably reflects a decrease in oxidative stress in the ejaculate.

Conclusion

Thus, the level of the main parameters of ejaculate fertility, characterizing the mobility and the number of normal forms of spermatozoa, shows a significant decrease in varicocele in the examined adolescents and adults at the preoperative stage. The failure of the operation in adult patients with varicocele can probably be associated with a low preoperative level of sperm motility and, possibly, with a short follow-up period. In adolescents, surgical correction, in most cases, gives a positive result.

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